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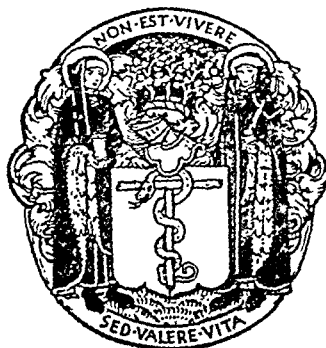
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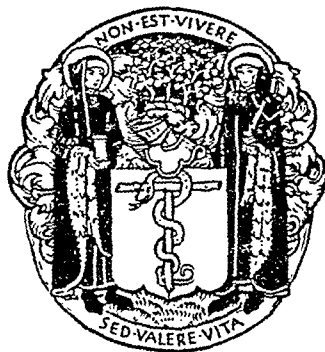
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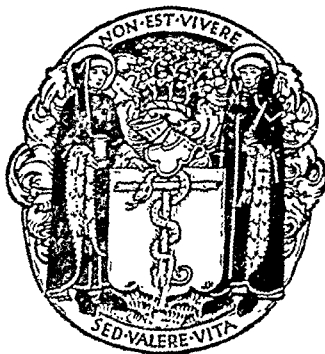
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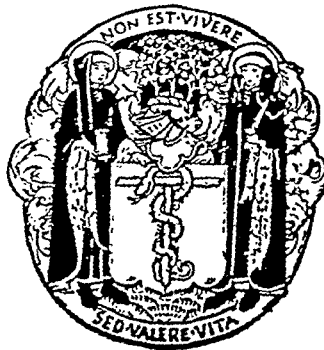
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Section of Otology with Section of Laryngology

COMBINED SUMMER MEETING HELD IN BRIGHTON

OTOLOGICAL SESSION

[June 27, 1947]

Chairman—H. V. FORSTER, M.C., M.B., Ch.B., M.Sc.

(President of the Section of Otology)

DISCUSSION ON THE ASSOCIATION OF OTITIS MEDIA WITH ACUTE NON-SPECIFIC GASTRO-ENTERITIS OF INFANTS

Miss Winifred Hall: Acute non-specific gastro-enteritis of infants, or the diarrhoea and vomiting syndrome, as it is also called, is recognized as a condition limited to the first twelve months of life. That is not to say that older children do not suffer from diarrhoea and vomiting, but the character of the disease and the behaviour of the patient are then quite different from what is seen in the infant. In infancy, the dominant feature of the severe case is the appalling dehydration, which may occur either with the primary disease, or as the herald of the onset of a parenteral infection. In the toddler and older children, dehydration is absent. Why this should be, we do not know. Whether we are dealing with a specific infection, bacterial or virus, but limited in its application to the first year of life, or whether it is something inherent in the gradually evolving economy of the young infant, has yet to be decided. Quite possibly it is a mixture of both factors. It is certain that the younger the infant, the more typical is the course of the illness, and after roughly 10 months of age the response of the child to its infection tends to approximate more and more to that of its elders. This means, therefore, that the approach of the doctor, which includes the otologist, to the problems of infantile gastro-enteritis must be quite different from his approach to illness in an older child.

† In Table I the incidence and mortality of cases admitted to the North-Western Hospital in

TABLE I.—NORTH-WESTERN HOSPITAL

Year	0-3 months		3-6 months		6-9 months		9-12 months		Totals		Mastoid operations	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
1942	40	12	19	10	9	3	6	4	74	29	—	—
1943	51	7	52	10	31	2	13	—	147	19	12	5
1944	72	17	87	13	33	4	28	3	220	37	27	4
1945	106	23	113	12	64	15	47	4	330	54	24	9
1946	82	10	87	8	39	3	34	2	242	23	6	1
1947	54	6	44	3	33	—	22	2	153	11	—	—

(to June 6)

the different age-groups during the years 1942-47 are shown, and the falling off of admissions in the later groups is very noticeable. The table also shows the very marked improvement in mortality figures in the later years. In 1942 the mortality rate was 39%. In 1943 it dropped to 13%. In 1943 the otitis media figures were 40% of all cases, yet you will notice that only 12 mastoid operations were done that year. In 1945 there were 24 operations; in 1946, 6; while for the first six months of 1947 there have been none. But, although both the otitis media rate and the mortality rate have fallen, the severity of the disease has in no way declined. The improvement is entirely due to better methods of general treatment, plus earlier recognition and more vigorous treatment of associated parenteral infections.

During the years 1942-47 I was attached to six hospitals in widely separated areas, and was therefore able to observe not only variations in the disease in the different localities, but also the results of varying paediatric treatments. Four of these hospitals were in London, and two at St. Albans. The total number of mastoid operations done during these years is 190, and several hundred more cases of otitis media were seen which recovered without operation.

The work on these cases began originally with the theory that the condition was a primary mastoiditis with a secondary irritative gastro-enteritis, a theory which has been postulated by various observers, and so in the early cases, all which failed to respond quickly to treatment proceeded to operation. We had, therefore, two main ideas in mind: (1) To

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pearance. A pink, or red, flush without fullness is not usually an indication for myringotomy; with adequate treatment such a drum may return to normal. It does indicate an incipient infective process that needs watching. I would consider the indications for myringotomy to be: (1) A localized grey or red posterior bulge; (2) a generalized red bulging drum; (3) a grey opaque bulging drum; and (4) a red flushed drum without fullness, but associated with pyrexia or an exacerbation of the general symptoms.

In the infant, the eustachian tube is short and straight. Cases have been recorded where milk has been found in the middle-ear cavity at operation. It is therefore important clinically that the babies should not be fed lying on their backs.

My first group of cases occurred in the latter part of 1942 at Oster House E.M.S. Hospital, St. Albans. At that time ordinary otitic conditions were very prevalent, and when our first cases showed a purulent otitis media early in the illness, and rapidly went on to operation with positive results, it did look as though the gastro-enteritis was merely the infant's way of responding to an otitic invasion. But as the series proceeded, and I began to extend my observations to other hospitals, it soon became obvious that this was not the case, and that the otitis was only an incidental factor in the disease. The onset of other parenteral infections produced exactly the same gastro-enteritic reactions as did the otitis.

The Oster House children were all examined aurally on admission. An abnormal drum was incised as soon as it appeared. Intravenous drips were used for the dehydration, but if no improvement occurred in forty-eight hours, we proceeded to a bilateral mastoidectomy. The reason for this was as follows: We found that in almost all cases of true infection, both mastoids were involved; and, further, the contents of the mastoids often bore no relation to the appearance of the drum. Often what appeared to be the better ear had the worse mastoid on operation.

Because of the absence of typical signs, the diagnosis of a mastoid infection and the decision when to operate can be extremely difficult. One of the most trying things from the surgeon's point of view is the way in which a purulent otitis will dry up. It is quite common to find a bulging drum, obtain pus on myringotomy with relief to the symptoms, and then have another general relapse in a few days' time. On examination the original incision is soundly healed, and the drum again red and bulging. In the early days I would have operated with such a history. Nowadays, I would not unless the child's condition continued to deteriorate in spite of treatment. I think that a certain amount of pus must escape down the eustachian tube, and after the immediate tension has been relieved by a myringotomy, the drum will therefore heal. If, later on, another sudden collection of pus occurs, the process is repeated. The myringotomies do not seem to have any untoward after-effects, and it is not necessary to open the mastoid after two or even three incisions, unless the general condition fails to respond. It must be remembered that a collection of pus in the middle ears can appear quite suddenly, and be accompanied by equally sudden symptoms. Within a few hours a normal drum can become red and bulging, and a fairly well baby become acutely shocked and dehydrated, with a disconcerting increase in its diarrhoea and vomiting; particularly its diarrhoea. At the same time it must not be forgotten that otitis is not the only infection that will cause these sudden general signs; pneumonia, for example, is a very common cause, and in cases where the indications are not clear, other infections must be excluded before placing the blame on the ears. If, after excluding everything else, there is still a doubt about the ears, they should be explored. The risk of a quick exploration, with a local anæsthetic, is very much less than the risk of an undrained infection.

The indications for operation are:

- (1) Persistent pyrexia.
- (2) Persistent, or increasing diarrhoea; this is a much more reliable indication than vomiting.
- (3) Sudden, or recurrent dehydration.
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Associated with a history of recent positive myringotomies.

- (5) Persistent, possibly profuse, otorrhoea associated with any of the above.

If any of the above persist in spite of strenuous general and anti-infective measures, then the mastoids should be opened.

- (6) As an exploratory measure in refractory cases, where no cause can be found for the symptoms, to exclude the possibility of a silent mastoid, remembering that with modern methods of treatment these cases are nowadays very rare.

Operative Procedure.

Until 1944, I operated with general anæsthesia, but it was found that no matter what the anæsthetic, chest complications were not uncommon; the babies tended to be collapsed afterwards, and took longer to recover, and the resumption of normal feeding was delayed.

determine whether in the acutely ill baby a mastoid infection was always to be found ; (2) To find out whether operation did or did not bring about improvement.

We soon found that the idea of a primary mastoid infection was untenable. By no means all severely ill babies even have an otitis media. But in those cases which had a mastoiditis, particularly where frank pus was found, improvement after operation was immediate and often dramatic.

In small babies the textbook signs of acute mastoiditis are completely absent. There is never any redness or swelling, and as a sick baby cries with any handling, it is quite impossible to know whether tenderness is present or not. The head-rolling sign, so often quoted, is quite unreliable, and so is enlargement of the posterior cervical group of glands. The drumhead signs can also differ from those of acute otitis in an older patient, due to differences in the anatomy of the infantile ear. It is advisable, therefore, before going on to the clinical aspect to consider these anatomical peculiarities, and the resultant difficulties in examination.

Anatomical Points.

One of the most important points is that in the infant the meatal canal runs downwards and forwards at an inclination of 35 degrees, so that in introducing a speculum one sees first of all the posterior and superior parts of the drum, and to see the anterior portion, it is necessary to tilt the speculum quite considerably. Ignorance of this can be a very real pitfall for those unaccustomed to the infant ear. Another point is that the calibre of the canal varies from the extremely narrow to the respectably wide; a variation peculiar to the individual, and in no way connected with his age.

In Lederer's "Diseases of the Ear, Nose and Throat" (1946 Ed., Philadelphia), we are told that in order to see the drum the speculum must be inserted until it nearly reaches the membrana. This is quite unnecessary, and will only cause damage to the meatal wall and drive the wax which is always present down on to the drum. A small speculum, carefully inserted and moved so as to show all parts of the drum in turn is all that is required. Wax is always present in the meatus in varying amounts. It must be completely removed before an accurate picture of the drumhead can be obtained, and this can be a very slow and difficult procedure. I personally use either a specially made fine hook, with a carefully rounded end, or the wool-carrying end of a very fine Jobson Horne wool carrier.

Contrary to the textbook statements the normal infant drumhead should show a properly formed light reflex, after about 6 weeks of age. It is usually shorter and fatter than in the adult, but it is quite definitely present, and absence means that the drum should be watched. Absence is not an indication for myringotomy, but it will be found that as the child returns to normal, so the light reflex reappears. I think that the reason why it is so often said to be absent in the infant is due partly to the anatomical difficulty of seeing that area of the drum, and partly to the difficulty of completely removing the wax. It is very easy to mistake a thin colourless deep-lying sheet of wax for the drum.

The tympanic membrane of an infant is said to be thicker than in later life. This is only so in the very young infant of the 1 to 6 weeks age-group; it is certainly not so in older babies. In the early days when we were doing many myringotomies as diagnostic measures in cases of unexplained pyrexia, or persistent toxæmia, one sometimes went through a thick opaque membrane, and had a dry puncture, while in other children of the same age-group, the drum would be quite thin, and the knife go through with the characteristic sound and feel of parchment. There does not seem to be any definite age when the change in character of the drum takes place; it seems to be an individual matter. The thick drums do not, of course, show a light reflex.

In the young infant there persists an undifferentiated mass of mesenchymal tissue in the upper part of the middle ear, often with trabeculae passing downwards to other points in the cavity. This mass partly shuts off the lower and anterior parts of the middle ear, and it is quite possible that it accounts for at least some of the cases of mastoiditis with an apparently normal drum. These cases, by the way, are not common, but they do occur, and the possibility of a completely "silent" mastoid must be remembered when searching for the cause of a persistent pyrexia, or a sudden collapse. It probably does account for the frequency with which one meets a suppurative otitis media confined to the upper and posterior part of the tympanic cavity. The auriscopic appearances in such cases are typical. There is an elongated red shining bulge along the posterior meatal wall, more marked above than below. On looking round, the drum proper appears to be lying on a much deeper plane, and often appears perfectly normal, even to the possession of a light reflex. The inexperienced observer is apt to assume that he is looking at a posterior wall furuncle. Actually the forward bulge of the posterior part of the drum carries with it the adjacent part of the posterior meatal wall, and it is often very difficult to make out where one ends and the other begins.

The appearance of the inflamed drumhead may vary from a faint greyish-red flush either at the margin, or spread over the surface, to the typical bulging bright red drum. Sometimes a tense collection of pus gives the drum a characteristic opaque grey colour, and full ap-

pearance. A pink, or red, flush without fullness is not usually an indication for myringotomy; with adequate treatment such a drum may return to normal. It does indicate an incipient infective process that needs watching. I would consider the indications for myringotomy to be: (1) A localized grey or red posterior bulge; (2) a generalized red bulging drum; (3) a grey opaque bulging drum; and (4) a red flushed drum without fullness, but associated with pyrexia or an exacerbation of the general symptoms.

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My first group of cases occurred in the latter part of 1942 at Oster House E.M.S. Hospital, St. Albans. At that time ordinary otitic conditions were very prevalent, and when our first cases showed a purulent otitis media early in the illness, and rapidly went on to operation with positive results, it did look as though the gastro-enteritis was merely the infant's way of responding to an otitic invasion. But as the series proceeded, and I began to extend my observations to other hospitals, it soon became obvious that this was not the case, and that the otitis was only an incidental factor in the disease. The onset of other parenteral infections produced exactly the same gastro-enteritic reactions as did the otitis.

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Because of the absence of typical signs, the diagnosis of a mastoid infection and the decision when to operate can be extremely difficult. One of the most trying things from the surgeon's point of view is the way in which a purulent otitis will dry up. It is quite common to find a bulging drum, obtain pus on myringotomy with relief to the symptoms, and then have another general relapse in a few days' time. On examination the original incision is soundly healed, and the drum again red and bulging. In the early days I would have operated with such a history. Nowadays, I would not unless the child's condition continued to deteriorate in spite of treatment. I think that a certain amount of pus must escape down the eustachian tube, and after the immediate tension has been relieved by a myringotomy, the drum will therefore heal. If, later on, another sudden collection of pus occurs, the process is repeated. The myringotomies do not seem to have any untoward after-effects, and it is not necessary to open the mastoid after two or even three incisions, unless the general condition fails to respond. It must be remembered that a collection of pus in the middle ears can appear quite suddenly, and be accompanied by equally sudden symptoms. Within a few hours a normal drum can become red and bulging, and a fairly well baby become acutely shocked and dehydrated, with a disconcerting increase in its diarrhoea and vomiting; particularly its diarrhoea. At the same time it must not be forgotten that otitis is not the only infection that will cause these sudden general signs; pneumonia, for example, is a very common cause, and in cases where the indications are not clear, other infections must be excluded before placing the blame on the ears. If, after excluding everything else, there is still a doubt about the ears, they should be explored. The risk of a quick exploration, with a local anæsthetic, is very much less than the risk of an undrained infection.

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Operative Procedure.

Until 1944, I operated with general anæsthesia, but it was found that no matter what the anæsthetic, chest complications were not uncommon; the babies tended to be collapsed afterwards, and took longer to recover, and the resumption of normal feeding was delayed.

I therefore started using 1% procaine as a local anaesthetic with some sort of premedication. Various drugs were tried, nembutal, seccional, chloral, but all were uncertain in their action, particularly if the child was still vomiting. The textbook dose of chloral as 1 grain per year of life is too small; the infant can tolerate much more than this. Chloral has one big disadvantage: occasionally it has a delayed reaction, and the child suddenly becomes pale, collapsed, and almost comatose two or three hours after it has been given. Seccional is the most satisfactory of oral sedatives. Nowadays, I use none of these but give morphia in the proportion of 1/40 grain per 14 lb. (0.00025 gramme per kilo) of body-weight. To give 1/40, for example, 1/4 grain (0.016 gramme) is dissolved in 10 c.c. water, and 1 c.c. is injected. It is essential to see that adequate time is allowed for the morphia to act before the child is taken to the theatre, and also that it is not disturbed in any way.

If two or three minims of adrenaline are added to the procaine, a bloodless field is obtained. 1 c.c. of procaine is used for each side. After injecting the superficial tissues the needle is plunged straight down on to the bone to infiltrate the periosteum. This can then be dissected off the bone and not scraped off. The baby does not mind a well-infiltrated periosteum being dissected away, but it does object to scraping.

Using a Bard-Parker number 18 knife a straight incision about an inch long should be made close to the post-auricular sulcus, and well above the mastoid tip. A longer incision than this only exposes an unwanted area of bone, and provided a sufficiently small retractor is used, the exposure is adequate. The subsequent scar is practically invisible, whereas if the usual long curved incision is made the result is both obvious and ugly. The bone must be opened widely; mere drainage down to the antrum is not enough. I have seen cases where this has been done without relief, and subsequent reopening showed extensive disease still present. The anatomical findings in these mastoids vary considerably, but it is evident that pneumatization can occur at a much earlier age than is taught. I have seen a completely pneumatized mastoid at 4 months old. The zygomatic cells seem to be the first to appear, and the apical cell the last. I have seen pneumatization in the zygomatic area at 4 weeks old.

I do not suture the wounds at all, but pack with half-inch ribbon gauze steeped in katiodine and parasepsin emulsion. Parasepsin is active against the usual pyogenic organisms, while katiodine, an electro-positive solution of iodine, is said to be active against the Gram-negative group, particularly the coliforms. This is most useful because of the frequency with which the latter appear either as contaminants or as active agents.

In that early series at St. Albans, we went very largely on failure to respond after forty-eight hours. All the babies were gravely ill on admission. The first 2 cases were not operated on, but at post-mortem the mastoids contained pus. The first 9 cases were done under general anaesthesia. 2 died with persistence of toxæmia and dehydration. Of the others, 4 made rapid and satisfactory recoveries after operation; the remaining 3 were held back by other infections, which in 2 of them was a post-operative pneumonia. Looking back on these cases one is struck by the fact that they were all cases of otitis media and mastoiditis from the beginning. That has by no means been the case in other series; presumably the organisms then responsible had a strong affinity for the ear. Taking all my cases, it is obvious that the idea of a primary otitis is quite untenable. In 1943-44, the otitis media rate at the North-Western Hospital was 40% of all cases. In 1945, the figures at the North-Eastern Hospital were 16%, and in 1946 29%. Although these are two different hospitals, they are all London cases, and the figures were compiled by the same observer. The fall in the number of ear infections is particularly interesting when one finds that the incidence of other parenteral infections, notably pneumonia, has not shown a corresponding fall.

Table II, which has been provided by Dr. M. Alexander of the North-Eastern Hospital

TABLE II.—NORTH-EASTERN HOSPITAL

1945 admissions	Associated with dehydration			Not associated with dehydration			Total cases
	On admission	After admission	Total	On admission	After admission	Total	
Parenteral inf.	53	27	80	70	29	99	= 179
Ot. media	10	8	18	9	10	19	= 37
Myringotomies	8	6	14	9	10	19	= 33
Mastoids	—	1	1	—	1	1	= 2

On admission = within seven days of commencement of illness.

brings out this point very well. It shows that in 1945, while there were 179 cases with some other form of parenteral infection, mostly pneumonias, there were only 37 cases of otitis media.

There is another very interesting parallel to this fall in the otitis media rate. In 1943 there was a big measles epidemic, associated with a very high otitis media rate. In the 1945 epidemic the otitis rate was low. This suggests very strongly that the otitic incidence in gastro-enteritis is a variable quantity, and fluctuates as the incidence in other diseases. In other words, if

in any given year there are at large a number of virulent organisms with a predilection for the ear, there will be a high otitis rate in diseases such as gastro-enteritis whose mode of onset is usually so devastating that the child's resistance is completely knocked out. If the attack is severe, these babies on admission are in a state of acute shock, and it is reasonable to assume that they are thereby rendered more vulnerable to whatever type of secondary infection happens to be about at the time. No doubt this variation explains why surgeons who have only recently begun to deal with these babies are not finding the mastoid infections that they had expected. Another point is that the death-rate has steadily declined. In 1942 at one hospital it was 39%; in 1946 it was 9.5%. Table III shows this very clearly.

TABLE III.—NORTH-WESTERN HOSPITAL

Year	Total admissions	Deaths	%	Mastoid operations	Deaths
1942	74	29	39	—	—
1943	147	19	12.9	12	5
1944	220	37	16.8	27	4
1945	330	54	16.3	24	9
1946	242	23	9.5	6	1
1947 (to June)	153	11	7.1	—	—

My largest series of operations at any one hospital was at the North-Western Hospital, with 69 cases for the period 1942-47. In this series there were 50 recoveries, and 19 deaths, an operation mortality rate of 27%. The cases have been classified according to the operation findings. Positive findings mean frank pus. Plus-minus means hyperæmia, or a little sticky mucus. Negative means that the ear was apparently normal. All cases had both ears opened, and the classification refers to the worse ear. As both ears were opened deliberately, irrespective of the signs, there were a certain number in which one ear was negative, but as I have already said one should never omit examination of a doubtful ear. The fact that nearly all the mastoids are bilateral is extremely interesting, and taking into consideration those cases where the infection is limited to the posterior part of the drum, there may have been in some instances at least a blood-stream infection.

Table IV shows the cause of death in the 19 fatal cases. In 10, there were no P.M. signs

TABLE IV

19 deaths

19 deaths

Causes	{	Toxæmia {	+ Operation findings, 6
			± Operation findings, 3
			- Operation findings, 1
		Pneumonia, 6 (all operation findings +)	
		Septicæmia, 3 (one with meningitis)	
			(operation findings +)

other than those of extreme toxæmia. In only one of these was there no operation evidence of otitis. The others died in spite of operation, the original infection in the toxæmic deaths, or the other parenteral infection in the others being presumably too severe to be overcome by drainage of the mastoids. It does not appear either, in looking through the notes that earlier operation could have saved the children. There is no evidence of undue delay. The post-operative progress varied. In some of the cases there was a short initial improvement, followed by a sudden collapse and rapid decline; in others there was no improvement, the child merely went on steadily deteriorating, with persistent gastro-enteritic symptoms.

Of the 50 recoveries, 3 had completely negative findings, and can be ignored. 22 made quick and convincing recoveries, while 25 recovered slowly. The 22 good cases all had mastoiditis as their only parenteral infection. 19 of them had frank pus in the mastoids. 3 of them merely showed a bony hyperæmia, but the improvement after operation was quite as rapid and convincing as in the others.

Of the 25 slow cases, 2 had to have the mastoids reopened to drain a residual area of infection, after which improvement was rapid. Of the other 23, 12 had a second parenteral infection, usually pneumonia, while in 11 no parenteral infection could be found, and the patients merely recovered slowly, with gastro-intestinal relapses of varying severity.

On the whole, figures from other hospitals agree with these. The number of negative findings was greater in the early days when we had less experience in the proper selection of cases for operation.

The conclusion to be drawn from this series is that where otitis is the only complication, an immediate and convincing recovery is to be expected. The first signs of recovery are cessation of the diarrhoea and vomiting, and no more dehydration, though this takes a little

longer to disappear. Delayed recovery after positive operation findings means either a second parenteral infection, or a degree of toxæmia too severe for the child to overcome except with difficulty.

The bacteriology of these cases is varied and confusing. Unless a secondary parenteral infection is present, many of the children go through their illness, and either die or recover without any organisms being found to account for their condition. True, they nearly all have inflamed throats, but the fact that something can always be recovered from the nasopharynx is no proof that the extremely varied and changeable flora there is responsible for the illness. Bacteriological examination of the stools and vomit has proved negative. The organisms found in the mastoids rarely coincide with those found in the throat, or even with each other. It is not at all uncommon to grow, for example, a streptococcus from one mastoid, and a pneumococcus from the other. I remember one child who grew a pure culture of *Str. viridans* from her throat. One mastoid gave a pure culture of the *Str. hæmolyticus*, and the other a pure culture of pneumococci. The child herself had a *Str. viridans* septicæmia.

The coliform bacilli play a very variable part. When a genuine pyelitis is present—not a common complication—they are usually responsible. They are often present in the nasopharynx, and are a very common contaminant on the skin surrounding the mastoid area. Hence the uselessness of penicillin as a local post-operative measure. Used by itself systemically, penicillin has been disappointing in the past. It has no effect on the gastro-enteritis itself, and will only control parenteral infection in the absence of the coliforms. We had an unpleasant instance of this at St. Albans. When penicillin first became available it was given to the gastro-enteritis cases. Unfortunately the administration coincided with the appearance of an extremely virulent strain of *B. coli*. 5 of the babies died, and we discovered too late that they were all *B. coli* septicæmias. I saw some similar cases at my other E.M.S. hospital, and there were also 2 cases at the North-Western Hospital. These 2 were fortunately discovered in time, and with sulphonamides the children recovered. The reason for the poor results with penicillin formerly, apart from coliform infections, appears to have been inadequate dosage. When the drug was first in use, 20,000 units four-hourly were considered a full dose for a 6-months-old baby. Nowadays one would give much more than that: 100,000 units six-hourly is quite a usual dose, and the response is correspondingly better.

Of the sulpha drugs all have been tried, and sulphathiazole and sulphadiazine seemed the most useful. It should be remembered that the infants' toleration for these drugs is much greater proportionately than that of the adult, and they can take surprisingly large doses. A combination of penicillin and a sulpha drug will give better results than either singly, particularly in the presence of coliforms.

Anæmia can be severe, and may greatly delay recovery. A small transfusion of whole fresh blood immediately after operation may make all the difference to the child's response.

Various investigators have suggested other sources of infection as the origin of the illness, for example the sinuses, particularly the posterior group. Others have found an œdematous condition of the brain and meninges, and have suggested that the condition is primarily an encephalitis. I have no personal knowledge of sinus findings, but cannot believe that a sinus infection is any more likely to be a primary condition than an otitis. As for the so-called encephalitis, physicians in this country, while agreeing that an œdematous appearance is often seen post mortem, do not consider that it is a true encephalitis, or that it has any causal significance.

Summary.—We still do not know the cause of acute infantile diarrhœa and vomiting. It is not bacterial, and it is not a primary mastoiditis. Many workers suspect a virus, a very tempting theory, but one which still has to be investigated. Mastoiditis undoubtedly occurs as a complication, and when the only one, response to operation is rapid and conclusive. The signs of acute otitis and mastoiditis differ in the infant from those seen in an older patient, but the effect is much more devastating, and the absence of redness and swelling must not be taken as an indication of a mild infection. If it is not treated promptly, the child will die before the stage of redness and œdema is reached.

One theory of the diarrhœa and vomiting is that it represents a "trigger response" to some stimulus. The initial one may be a virus or some other unknown quantity, but the response once started can then be elicited by any subsequent stimulus, of which otitis media is one. It takes very little to set the syndrome off once the illness has started, and a mild otitic infection could certainly do so, but a mild otitis does not as a rule go on to a mastoid infection.

An interesting point about this trigger-like irritability is that it seems to persist for some time even after apparent cure, and a baby discharged from hospital as perfectly well may be back in a few days' time as bad as ever.

Repeated myringotomy, or operation, does not appear to have any ill-effect on the hearing, unless operation has been delayed too long, in the presence of a severe infection.

I only know of two cases of severe deafness following mastoiditis, and in both of these there was an extensive bilateral purulent infection which, because of the absence of local signs, was not recognized as mastoiditis until the occurrence in one case of a facial palsy, and in the other a meningitis, superimposed upon a profuse persistent ear discharge led to the summoning of an otologist. Both these children are now at a school for the deaf.

Postscript.—The peak years for my cases were 1943 and 1944. In the first half of 1947 I saw very few cases of otitis media, and did no operations. But now, in December, it would appear that we are about to experience another upward swing in the otitis media rate. There has been a marked increase in the number of otitic cases in the last two months, and in their severity. As the occurrence of otitis media in gastro-enteritis is definitely seasonal, being at its height at the same time of year as otitis in other complaints, this strongly suggests that this winter is going to show a large number of ear complications. What effect present-day pædiatric treatment plus the administration of sulpha drugs and penicillin will have on the incidence of mastoiditis remains to be seen.

I should like to express my thanks to all my colleagues whose cases have formed the basis of this paper, particularly Dr. William Gunn of the North-Western Hospital, and Dr. M. Alexander of the North-Eastern Hospital, whose notes and statistics I have used.

Mr. John E. G. McGibbon: In view of Miss Hall's comprehensive account of the syndrome of acute otitis media, latent mastoiditis and diarrhæa and vomiting in infants, I propose to base my remarks on observations made on a series of patients who have been under my own care during the past sixteen months.

Incidence.—The frequency of infection of the middle-ear tract in infants is still not appreciated, and until recently the most striking evidence of the prevalence of such infection came from the post-mortem room.

Ebbs' (1937) figures are frequently quoted. He stated that 368 (61%) of 603 infants who died whilst suffering from diarrhæa and vomiting were found at autopsy to be suffering from a purulent infection of the middle-ear cleft.

Coupar and McConkey (1937) found that, in 1936, of 1,324 infants under 1 year of age admitted to Alder Hey Children's Hospital, Liverpool, 195 (14%) suffered at one time or another from otitis media, or otitis media and mastoiditis, and an analysis by Derham (1947) shows that 240 (21.6%) of 1,107 infants admitted to the hospital in 1946 were suffering from aural infection when first examined, and that 191 (17.2%) developed a lesion of the middle-ear cleft after admission—making a total of 431 (39%) infants with ear disease, and in 193 (44.7%) of these cases this was associated with diarrhæa and vomiting.

Material used in the following notes.—During the sixteen months from September 1945 to December 1946, 104 infants suffering from diarrhæa and vomiting were operated on for latent mastoiditis in this hospital; and during the same period, 32 infants, who died of diarrhæa and vomiting and who were unsuspected of mastoiditis during life, were found to have a purulent infection of the tympanic cavities and mastoid antra at autopsy. I think it may be assumed that during this period there were more infants who died with unrecognized mastoiditis who did not come to post-mortem.

The following observations are based on the records of 67 of these patients operated on personally—all of whom were suffering from diarrhæa and vomiting when seen by me—and of the 32 cases found at autopsy to have suffered from undiagnosed infection of the mastoid antra, making a total of 99 cases.

The figures quoted are for comparison only and are of no statistical value.

The average age of the infants operated on was 4.3 months, and of the undiagnosed cases it was 3.6 months. Two of the undiagnosed cases were under 1 month of age.

Ætiology.—The ætiology of the syndrome is illustrated diagrammatically in fig. 1.

Diarrhæa and vomiting (1, fig. 1) may result from:

(a) *Enteral infections* (2, fig. 1), i.e. a true gastro-enteritis, which may be bacterial or caused by a virus. In the present series, rectal swabs were negative in 66.6% of the cases so examined (Table I) and the weight of evidence to-day is in favour of a virus infection (*Lancet*, 1947).

TABLE I.—BACTERIAL FINDINGS IN RECTAL SWABS OF 66 PATIENTS

	Positive (<i>B. proteus morgani</i>)	Negative	Total
Survivors	7 (31.8%)	15 (68.1%)	22
Fatalities	5 (21.7%)	18 (78.2%)	23
Undiagnosed	10 (47.6%)	11 (52.3%)	21
Totals	22 (33.3%)	44 (66.6%)	66

Pathological changes in the bowel were found in only 10 (27%) patients of 37 who were examined post mortem—i.e. only about a quarter of these cases were suffering from a true gastro-enteritis (Table II).

TABLE II.—CHANGES IN THE BOWEL FOUND AT POST-MORTEM IN 37 INFANTS

Fatalities	Positive (Distension, hyperæmia pseudo-membranous inflammation, hæmorrhage or hæmorrhagic contents)		Total
	Nil (Nil)	Negative	
Undiagnosed	10 (35.7%)	9 (100%)	9
		18 (64.3%)	28
Totals	10 (27%)	27 (73%)	37

There is evidence that in both sporadic and epidemic cases of infantile gastro-enteritis changes are found in the brain which are characteristic of an infection by a virus.

(b) *Parenteral infections* (3, fig. 1) such as otitis media, pneumonia, pyelitis, cellulitis, erysipelas, &c.

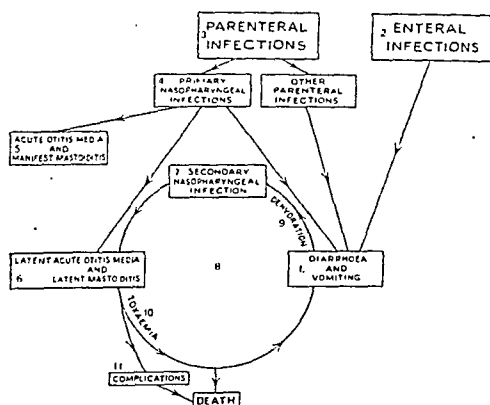


FIG. 1.—The syndrome of acute middle-ear cleft infection, mastoiditis and diarrhoea and vomiting in infants.

In 1930 Marriott wrote in the introduction to his book that: "Many of the disturbances of infants which have previously been attributed to dietary faults are in reality the results of infection" . . . and that "the most frequent infections that interfere with nutrition are otitis media and pyelitis" . . . and it is now generally recognized that vomiting and diarrhoea may occur in infants suffering from any acute infection.

Otitis media and mastoiditis.—Infection of the middle-ear cleft is usually secondary to nasopharyngitis, and it is caused either by direct entrance of organisms along the eustachian tube—some observers have stated that they have found ingested milk in the mastoid antra—or by lymphatic spread.

If blood-borne infection of the middle-ear cleft does occur in infants, the number infected in this manner must be very small.

Naso-pharyngitis may be due either to:

(a) *Primary* upper respiratory infection (4, fig. 1), which in the infant sometimes may be so slight and transitory as to escape recognition.

This may give rise to *manifest* acute otitis media and manifest mastoiditis (5, fig. 1) with swelling and redness over the mastoid process, which is an infrequent occurrence. It is a benign condition which causes little constitutional disturbance and which is cured by operation.

Or it may give rise to *latent* acute otitis media and latent mastoiditis (6, fig. 1) which will be described later.

(b) *Secondary* infections (7, fig. 1) caused by organisms deposited in the nasopharynx by vomiting and/or regurgitation.

It is obvious that vomiting can infect the nasopharynx, so that secondary nasopharyngitis may result from enteral or parenteral infections.

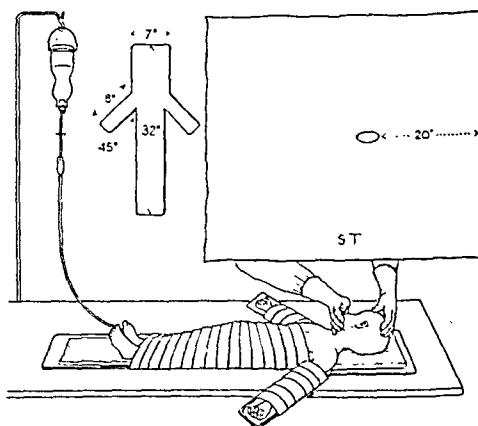


FIG. 2.—Diagram of special splint and towel. S.T.—special towel, 48 in. × 52 in. (See p. 11).

Fig. 1 demonstrates that none of the lesions mentioned can be regarded as a separate entity—all may be recognized as part of a syndrome—the *syndrome of acute otitis media, latent mastoiditis and diarrhœa and vomiting* which constitutes a vicious circle (8, fig. 1).

Vomiting and diarrhœa lead to dehydration (9, fig. 1), toxæmia (10, fig. 1) and other serious complications (11, fig. 1).

The vulnerability of the infantile middle-ear cleft may be explained partly by certain anatomical features whereby organisms in the nasopharynx can obtain easy access to the tympanum and antrum along the eustachian tube, or whereby drainage of the more distal portion of the cleft is impaired.

First the infant eustachian tube is shorter (14 mm.) than the adult tube (32-38 mm.); it is more horizontal, so that the level of the infant's tympanic floor is slightly below that of the floor of the nasal fossæ (in the adult it is 20-22 mm. above the hard palate), and its lumen is relatively greater than that of an adult.

Secondly the middle-ear cleft is developed from the tubo-tympanic recess which grows out from the primitive pharyngeal pouch into a mass of mesenchyme.

It is stated that in the infant tympanum there sometimes is a residue of the mesenchymal tissue in the region of the aditus which is not absorbed entirely until several months after birth; and it is possible that in some cases this residual tissue, as a result of infection, becomes swollen and blocks the aditus; this also may be one of the explanations of a dry myringotomy in some cases of latent mastoiditis.

Diagnosis.—The nomenclature of the disease from which the infants were considered to be suffering at the time of admission to hospital was dependent on the predominant symptoms present at the time, on the particular interest of the admitting Medical Officer, and on his ability to see the drumhead.

Thus, from the series of 99 infants known, or found, to be suffering from latent mastoiditis, the diseases noted on admission are shown in Table III, and it will be seen that 61 (i.e.

TABLE III.—DISEASES NOTED ON ADMISSION OF 99 INFANTS SUFFERING FROM LATENT MASTOIDITIS

Diagnosis on admission	Undiagnosed cases of mastoiditis found at autopsy			Total 99
	Survivors 36	Fatalities 31	32	
Gastro-enteritis	14	10	14	38
Gastro-enteritis and bronchitis	1	1	—	2
Gastro-enteritis and pneumonia	1	2	—	3
Gastro-enteritis and otitis media	4	6	1	11
Gastro-enteritis, pneumonia and otitis media	2	—	—	2
Gastro-enteritis and stomatitis	2	—	—	2
Vomiting	—	—	2	2
Vomiting and bronchitis	—	1	—	1
Otitis media	1	2	1	4
Septicæmia and otitis media	—	—	1	1
Bronchitis	5	1	1	7
Pneumonia	3	3	—	6
Pneumonia and vomiting	—	—	1	1
Pneumonia and otitis media	—	1	—	1
Pneumonia, otitis media and jaundice	—	1	—	1
Pneumonia and measles	—	1	—	1
? Meningitis	—	1	—	1
Marasmus	1	1	4	6
Marasmus and jaundice	—	—	1	1
Feeding difficulty	2	—	—	2
Abscess of arm	—	—	1	1
Pyloric stenosis	—	—	1	1
Infective hepatitis	—	—	1	1
Jaundice	—	—	2	2
Prematurity	—	—	1	1

61.1%) were considered to be suffering from diarrhœa and/or vomiting, and 20 (i.e. 20.2%) from otitis media, alone or in association with lesions of other organs.

If the drumhead is not normal the infant is certainly suffering from middle-ear cleft infection, and he may or may not have a latent mastoiditis.

The appearances of the drumheads on admission of 60 of the 67 cases submitted to operation were entered on the case-sheets, and, although in 39 (58.1%) infants one or both drumheads were noted to be abnormal, only on 20 (29.8%) of these case-sheets was otitis media included in the original diagnosis.

Symptoms.—Symptoms pointing to middle-ear cleft infections in infants may be few or absent.

Head-rolling, restlessness, fretfulness, screaming attacks, drowsiness and, in a few, convulsions, may be present.

Signs.—*General signs* are those of failure by infants suffering from diarrhoea and vomiting to respond to adequate general treatment.

The most urgent signs are persistent vomiting and diarrhoea with loose green stools, dehydration and loss of weight; particularly if these are associated with any considerable rise of temperature.

Local signs can be found only by otoscopic examination.

The drumhead may be lustreless, grey, crinkled, invaginated or full and congested. Occasionally sagging of the postero-superior wall of the meatus may be present.

Otorrhoea is not a frequent finding—it was noted in 6 (8.9%) of the 67 patients submitted to operation.

Latent mastoiditis should be *assumed* only if the symptoms do not improve after a dequate drainage of the tympanum has been established, either by spontaneous perforation or by incision of the drumhead.

Bacteriology and pathology.—Whether the diarrhoea and vomiting be caused by a virus or by bacterial infection, there can be no doubt that the mastoiditis is bacterial.

The organisms cultured from the mastoid antra of the 99 cases are shown in Table IV;

TABLE IV.—BACTERIOLOGICAL FINDINGS OF THE MASTOID ANTRA IN 99 CASES OF INFANTILE MASTOIDITIS

Organisms	Posterior drainages		Undiagnosed	Totals
	67			
	Recoveries 36	Fatalities 31		
Sterile	4	9	1	14
<i>Staph. aureus</i>	14	5	1	20
<i>Staph. aureus</i> and non-hæm. streps.	—	—	1	1
<i>Staph. aureus</i> and <i>Staph. alb.</i>	1	—	—	1
<i>Staph. aureus</i> , proteus and <i>Strep. fecalis</i>	—	—	1	1
Pneumococci	1	2	4	7
Pneumococci and proteus	1	—	—	1
<i>B. coli</i>	5	6	5	16
<i>B. coli</i> and <i>Staph. aureus</i>	1	—	—	1
<i>B. coli</i> and pneumococci	—	2	4	6
<i>B. coli</i> , <i>Staph. aureus</i> and <i>Strep. fecalis</i>	—	—	1	1
<i>B. coli</i> and <i>Strep. fecalis</i>	—	—	3	3
<i>B. coli</i> and diphtheroids	—	1	1	2
<i>B. coli</i> and non-hæm. streps.	—	—	1	1
<i>B. coli</i> , non-hæm. streps. and diphtheroids.	—	—	1	1
<i>B. coli</i> , hæmolytic streps. and diphtheroids.	—	1	1	2
<i>B. coli</i> , and <i>Staph. alb.</i>	—	—	1	1
<i>B. coli</i> and <i>B. influenzae</i>	—	—	2	2
Hæmolytic streps.	1	1	—	2
<i>Staph. albus</i>	6	2	—	8
<i>Staph. alb.</i> and diphtheroids	1	—	—	1
<i>Staph. alb.</i> and Friedlander	1	—	—	1
<i>Staph. alb.</i> and proteus	—	1	—	1
<i>B. proteus</i>	—	—	2	2
Hæmophilus group	—	1	—	1
Findings unknown or not cultured	—	—	2	2

and from this it may be seen that *B. coli* alone or with other organisms were obtained in 36 cases, of which 30 died; *Staph. aureus* were found alone or with other organisms in 25 cases, of which 9 died; and pneumococci alone or with other organisms were present in 14 cases, of which 12 died.

Hæmolytic streps. were present only in 4 cases, which is a surprisingly low figure.

It is interesting to note that only in 50% of the cases similar organisms from the meatus and mastoid antra were cultured.

The organisms found by culture from the antra are shown in column A of Table V, and I have compared them in column B with the bacterial findings in 92 cases of acute suppurative otitis media, not in infants, quoted by C. P. Wilson (1946). Both of these series occurred in the same period—i.e. 1945-46, so they are strictly comparable.

TABLE V

A (McGibbon)				B (Wilson)	
Infants with gastro-enteritis (99 cases)				Non-infants (92 cases)	
<i>B. coli</i> alone or with other organisms	36 (36.3%)	Nil	
<i>Staph. aureus</i> alone or with other organisms	25 (25.3%)	19	(20.6%)
Pneumococci alone or with other organisms	14 (14.1%)	18	(19.5%)
Hæmolytic strep. alone or with other organisms	4 (4.0%)	46	(50.0%)
Others	16 (16.1%)	6	(6.5%)
Sterile	14 (14.1%)	3	(3.2%)

Of the infants submitted to posterior drainage the best results were obtained in those from whom *Staph. aureus* were obtained by culture.

The fourteen patients from whom sterile cultures were obtained had all been subjected to intensive chemotherapy and systemic penicillin, which may have been the cause of the absence of bacterial growth.

When pus was present it was usually of a thick tenacious nature.

In all cases except two, the naked-eye pathology was confined to the mucoperiosteum; and the lesions observed were congestion and/or œdema of the mucosa and the presence of serous or purulent fluid.

In two patients only was there an obvious osteitis. Sections of bone were not made and the impression gained was that the antrum was a cesspool of pus which did not kill by toxæmia but by causing a persistence of the diarrhœa and vomiting (see fig. 1).

The absence of bone disease is borne out by the investigations of Causee (1946). He sectioned seventeen mastoid bones of 13 athreptic infants with mastoiditis and found no involvement of bone by infection.

Treatment.—General treatment is a pædiatric problem, and the amount of time, effort and skill in this respect that has been spent by the Resident Medical Officers and Nursing Staff on these patients has been unbounded.

There is one point that I would stress in regard to general treatment, and that is the importance of active measures to restore the fluid content of the body by the intravenous route—in dehydrated infants this is a most valuable pre- and post-operative measure; in some cases the infusion of whole fresh blood appears to be a life-saving procedure.

Systemic penicillin and sulphonamides do not appear to have any beneficial effect.

Local treatment.—If an infant with abnormal drumheads suffering from diarrhœa and vomiting fails to respond to general treatment, myringotomy should be performed.

In very many cases this marks the turning-point to recovery.

Sometimes there may be an audible "pop" on incision of the drumhead, which Le Mee (1937) considers to be due to air rushing into the tympanum; but in the presence of gas-forming organisms it may be due to the gas rushing out.

The products of myringotomy in 61 of the 67 cases operated on were as follows:

(1) *Dry incision* in 5 cases (8.2%). A dry myringotomy may be due to (a) dehydration—such a dry middle ear will discharge when the fluid balance of the infant is restored; or, as mentioned earlier, it may be due to (b) obstruction of the aditus by swollen mesenchyme.

(2) *Blood only* in 8 cases (13.1%). This may conceal any other fluid that may be present, or

(3) *Serous fluid or pus* in 48 cases (78.7%). This was the most frequent and satisfactory finding.

Preliminary myringotomy was performed in 61 of the 67 patients operated on by posterior drainage, and in 15 of these the drumheads were incised on more than one occasion.

After reviewing the cases, I am of opinion that valuable time may be lost by repeated myringotomies, as 10 cases (66.6%) of the 15 submitted to more than one myringotomy died; and I consider that if an infant does not improve within twenty-four hours after preliminary myringotomy, the mastoid antrum should be drained by the posterior route.

Posterior drainage is a simple operation carried out under local anæsthesia, after premedication with chloral and bromide.

I do not propose to describe the operative technique in detail.

Before operation the infant is bandaged to a splint (fig. 2, p. 8) and during the operation his head is held in position by a nurse, whose hands are covered with a towel with a small hole to leave exposed the ear and mastoid region.

After operation the antrum is lightly packed, and the wound is kept open and allowed to heal by granulation.

It may be necessary to insert one or more hæmostatic sutures which are removed in twenty-four hours.

Of the 67 cases drained in this manner, in 59 both mastoid antra were opened, and in 8, one antrum only was drained.

Of the 126 mastoid antra opened, 10 were macroscopically normal, but from 7 of these positive bacterial cultures were obtained.

As the unopened antrum was found to be infected at autopsy in 2 cases, and, as infection of both antra was present in 26 of the 32 cases of unrecognized mastoiditis, it has been my practice latterly to explore both antra at operation, if both drumheads were abnormal.

Convalescence often was stormy and extended over several months.

Results of operation.—The results of operation on paper are deplorable. 36 patients (53·7%) recovered, and 31 (46·3%) died, but I am convinced that without operation the mortality rate would have been over 90%.

The majority of patients came to operation as a last resort in regard to treatment; and they were, in fact, moribund at the time of operation; and I consider that these findings demonstrate the necessity of *early* operation if a preliminary myringotomy fails to bring about improvement of the infant's condition within twenty-four hours.

My thanks are due to Dr. W. E. Crosbie, Medical Superintendent of Alder Hey Children's Hospital and to the Resident Medical Officers; also to Dr. H. Lederer for the bacteriological investigations and Dr. Joan Gregory and Dr. Eileen J. Owens who abstracted the case-sheets.

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Was it the general rule to find otitis media on both sides, rather than in one ear alone?

Mr. H. S. Sharp said that in the two years 1944-46, 492 cases of gastro-enteritis were admitted to the Hospital for Sick Children, Great Ormond Street, upon 36 of whom bilateral mastoid operations were performed. These were done following paracentesis which did not lead to resolution of the otitis media. 9 myringotomies were also performed which *did* lead to resolution of the otitis media. Of the 36 bilateral mastoids, 30 were subjected to a detailed analysis in the endeavour to discover any pointer to help in diagnosis. Of these 30 cases, following the opening of the mastoid, 16 were found to have pus in the mastoid on both sides and 14 had clear mastoids. In other words, there was an error of practically 50% in the diagnosis. These cases were also subjected to a five-day white count done according to the Schilling method. This failed completely to assist in the diagnosis. In the 16 cases which had pus in the mastoid the average white cell count was 16,000, and in the 14 cases with no pus it was 18,000. The other point was whether the influence of penicillin had had anything to do with the production of a sterile culture from the mastoid. This again gave an indeterminate result. Altogether the investigations directed to forming some diagnostic criteria had not helped at all.

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little doubt about the respiratory infection, but he did not think there was any reason to concentrate on the ear. It was a respiratory infection that caused these troubles, and not necessarily an ear infection. It might be a pharyngitis or a sinusitis.

At Great Ormond Street they had been aware of the possible association of otitis with gastro-enteritis for many years. Every case presented problems of its own and when an aural operation was performed the indications for it were often less adequate than they would have desired. There was a class of case in which the physician declared that the child was dying and that he had done all he could, and suggested that there might be a hidden infection in the mastoids. The mastoids had sometimes been opened in such cases without any local indication at all, and pus had been found although there was nothing to indicate from the outside that it was present. Sometimes these babies seemed to have recovered as a result of this operation, which was simply an exploration.

The most usual clinical picture was that of the baby who came into the hospital with gastro-enteritis, and, often within a few days of admission, coinciding usually with an exacerbation of the diarrhoea and vomiting, the tympanic membranes were noticed to be abnormal; not the red bulging membranes of which Miss Hall had spoken, but dull drums, slightly pink and thick. Sometimes the baby improved after incision of the drum; at other times the improvement was only temporary, more vomiting and diarrhoea ensued, and then the mastoid was opened. In quite a number of these children pus was found in one mastoid or in both, and they were assured by the physicians and sisters alike that there had been immediate improvement. The cases which really troubled them were those in which they opened the mastoid and found nothing, and the baby started to get better. No one knew why—whether or not it was due to the new interest in the child—but it did happen.

He would not be prepared to say that infection alone in the ear could cause gastro-enteritis—he had seen so many babies with acute otitis media with not the slightest sign of gastro-enteritis. He had opened many acute mastoids in infants in whom there was no gastro-enteritis. He thought that mastoid infections were likely to occur in any debilitated baby that was vomiting as it lay on its back. In such a position some of the vomit passed into the short wide eustachian tubes, and he had actually seen milk in the mastoid antrum. When an infection did occur in the ear, as he had said, it made the child's gastro-enteritis worse. Sometimes they responded to incision of the ear drum, at other times to opening of the mastoid. It seemed quite certain that babies with diarrhoea and vomiting should have their ears examined daily. Any sign of inflammation in the drums called for paracentesis. He did not think the mastoid should be opened if there were no signs of inflammation in the ear. They had to go on such clinical signs as were apparent, and he would be doubtful about doing this operation just on the chance that some infection might be there.

Mr. Eric Watson-Williams said that in the last fifteen years he had seen rather less than 100 of these children. But he was quite convinced that a proportion of these had infective material in the antrum, and some of these children who seemed desperately ill certainly did recover after the infective material had been given artificial egress. Further than that he found it difficult to go. He rather supported the view that every reasonable measure that might tend to turn the scale should be undertaken. Mastoid opening in a small infant was not an operation of great severity. It was a matter literally of minutes—of very few minutes in fact—and he liked to feel that, unless the baby was over six months, he could complete the operation well inside five minutes. There ought not to be much shock.

He had been particularly interested in Miss Hall's remarks on periodicity. Periodicity in diseases was a most fascinating subject. He had analysed the periodicity of pneumococcal infections in the sinuses, and it was most extraordinary how waves of pneumococcal sinusitis in children were seen. For three or four years there would be very little, and then suddenly there would be a great deal. It was probably perfectly true that the virus turned up in waves (*Brit. med. J.*, 1929 (i), 720).

Mr. W. Stirk Adams said that Miss Hall had quoted figures which led one to hope that the medical treatment of the entity which they used to know, and still knew, as diarrhoea and vomiting was so improved that the mortality had been reduced from 30% of all cases as it was years ago to 9% last year. Whether that was because they had admitted to the hospital larger numbers of children in a less severe degree of illness they had not been told, but a study of the paper would be very useful to them all, and his comments at the moment must be tentative.

Mr. McGibbon appeared to have been dealing with a more severe type of case; and he had found otitis much oftener than Miss Hall. This difference was interesting and might be

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[June 28, 1947]

Chairman—H. V. FORSTER, M.C., M.B., Ch.B., M.Sc.

(President of the Section of Otology)

The Peep-Show Technique for Pure Tone Audiometry in Young Children¹

DEMONSTRATION AND FILM

By M. R. DIX, F.R.C.S., and C. S. HALLPIKE, F.R.C.P., F.R.C.S.

(*Otological Research Unit, Medical Research Council, National Hospital, Queen Square, London, W.C.1*)

Mr. Hallpike said that the test procedure to be described had been designed to solve the difficult clinical problem of the young child, under the age of 5 years, in whom backwardness was associated with failure of speech development. The failure might be due to deafness, to mental defect, or to a purely motor disorder of speech. The otologist was called upon for an authoritative opinion on the hearing, and here the question of a suitable test was a very difficult one. Ordinary speech tests were very difficult in the presence of deafness with defective vocabulary, while young children found pure tone audiometry very boring, and their responses were in consequence unreliable. A still greater difficulty attended the standard test procedure for pure tone audiometry; namely that before the test could be applied the child needed to be given and to assimilate an explanation of the nature of listening and hearing with the telephone receiver. This was often impossible. In designing the Peep-Show procedure they had endeavoured to overcome these difficulties: First, by giving an arresting significance in the child's consciousness to the usually uninteresting pure tone stimuli; secondly, by so devising the test that the child was persuaded to respond to the sound stimulus with no explanation other than a very simple dumb show.

Mr. Hallpike then demonstrated the test equipment and showed a short film of deaf children undergoing the test. He said that the method was of particular value between the ages of 3 and 6 years. With children of normal intelligence decisive results were nearly always obtained in the course of a single visit to the Clinic.

Miss Dix said that a vital point in the management of the children was that they should not be seen when tired or hungry. All cases were seen by appointment in a quiet room with their parents. It was essential not to attempt this in a busy Out-Patient Department. During the interview she played with the child while Mr. Hallpike talked to the parents while observing the child and assessing its intelligence. Only when its co-operation had been secured in this way did they proceed to the Peep-Show test.

Mr. Terence Cawthorne said that he had the advantage of having seen this device in action and of providing Mr. Hallpike with some deaf children to test. One of the most difficult problems in otology was a child under 5 who, though obviously hard of hearing for speech, was able to hear certain sounds. It was important, in such cases, to make a reasonably accurate estimate of the child's hearing. It might be labelled as requiring psychological treatment, or for education at a deaf school, when in fact it could quite well be educated with appropriate assistance with hearing children. Therefore any method of testing that gave a better and more accurate picture of the hearing capacity was of the greatest importance. Some of these children were very shy and would not respond to any form of sound at all, and yet one felt that there was some hearing. With the peep-show technique such children could be made to respond when all other methods failed.

¹For a full description of the test procedure and equipment reference should be made to the authors' article in the *British Medical Journal*, 1947 (ii), 719.

due to the conditions under which Mr. McGibbon worked and might correspond to the practice as they saw it in the Children's Hospital at Birmingham, where the physicians and pædiatricians were in charge of their patients, where there was a constant watch on the drumhead, and where they did their best for the patient, but called in the otologist to carry out the necessary treatment the moment there was any doubt about the ear.

The most important point was the time of intervention. It was highly disadvantageous to open the mastoid too early or too late—if too late there was secondary general infection and the case was hopeless.

Mr. G. A. Fraser said that they had had a rather severe outbreak of infantile gastro-enteritis in the Brighton area recently, and Mr. Allen and himself had had a very worrying time deciding upon which children they should do a mastoidectomy. During the last year 27 bilateral mastoidectomies were performed on babies suffering from gastro-enteritis. In half of these cases there were signs of middle-ear disease, but the other half showed no clinical signs of middle-ear or mastoid infection, and these cases were operated on only after a great deal of pressure from the physicians. The striking thing was that of the 27 cases operated upon only two were found to have perfectly healthy mastoid processes.

Miss Winifred Hall, in reply, said that most of her cases had been in the L.C.C. fever hospitals, where the majority of London gastro-enteritis cases were now sent, in preference to the general hospitals. Although a certain number of mild cases were sent in, the majority were very acutely ill, and while she could not give figures, it was quite certain that the fall in the death-rate was due to improved treatment, and not to a greater number of mild cases. She was strongly of opinion that the mortality of the disease had a great deal to do with the pædiatric treatment, and the greater the experience and care of the pædiatrician and nursing staff, the better were the results. In one hospital showing very good results the medical officer in charge of the wards had been dealing with nothing but gastro-enteritis for the last four years.

Mr. Crooks' point about the immediate and surprising improvement sometimes seen in babies with negative operation findings was important; she had seen it several times. Yet, in other apparently similar cases, there would be no improvement, and the child would die. She did not know any reason for this improvement. She had not found any laboratory procedures of help in making a diagnosis; she went on the lines given in the paper. Also when one had seen a number of these cases, one acquired a sixth sense about them which was quite as helpful as any sign. The white cell count was notoriously misleading. She did not know why in some cases of purulent mastoiditis an operation swab should be negative. It was not always due either to penicillin or to sulphonamides. It could occur in cases which had had neither. She had tried sending pieces of bone for culture, but even these were sometimes negative.

She did not use any form of splint at operation, merely wrapping the babies in a small blanket in the fever hospital method for tracheotomy. She had seen two cases of brachial palsy, fortunately only temporary, after the use of a splint, and was rather afraid of them. She thought myringotomy preferable to puncturing the membrane with Gray's needle. The incision healed very satisfactorily, often in twenty-four hours, and even after obtaining pus, so that there was apparently no reason to fear its remaining as a future source of infection.

As regards periodicity, at the moment in London they seemed to be at the bottom of the swing, but it might at any time come up again, and there were signs that it was now starting to do so (December 1947). She was against exploratory puncture of the mastoid antrum, on the grounds that this would not relieve extensive disease which would need further opening, but chiefly because it would miss pus confined to one or other of the groups of cells, and so mislead the operator. She had had several cases where the zygomatic cells only contained pus, and an antral puncture would not have touched them. One of the two cases that needed reopening showed zygomatic infection, and when this was cleared out, the child promptly recovered.

Mr. J. E. G. McGibbon, also in reply, said that in his hospital where there was a number of experienced medical officers, it was often difficult for them to arrive at an opinion as to the presence of mastoiditis on the appearance of the drumhead. Sometimes there was too much delay in calling upon an otologist to see the case, and he had heard of an infant who had four myringotomies in a period of about fifteen days. He felt very strongly that the babies who did not improve after myringotomy went down so quickly that they might be dead within forty-eight hours. The majority of the babies he saw were those in whom a myringotomy had not stopped their downward course. He thought that in such cases the mastoids should be opened within twenty-four hours and not left for forty-eight or seventy-two hours, by which time the baby might be dead.

Section of Obstetrics and Gynæcology

President—A. J. McNAIR, F.R.C.S., F.R.C.O.G.

[October 17, 1947]

DISCUSSION ON POST-OPERATIVE THROMBOSIS

Dr. Helen Payling Wright: The problem of venous thrombosis is a very serious one for the surgeon and midwife. It has been estimated that pulmonary embolism follows roughly 1:100 of all major surgical operations and that about one out of every six is fatal. The incidence of thrombosis is almost twice as common in females as in males and is most frequent after operations in which the abdominal cavity is opened and the pelvic viscera explored. It may, therefore, be of value to review the changes which occur in the blood in the days immediately following surgical operations, bearing in mind, also, that exactly similar changes occur after parturition, though in these cases the trauma is caused by excess pressure and bruising of the pelvic tissues and not by their section.

The main chemical changes which occur during the post-operative period are a rise in fibrinogen content of the plasma and an increased activity of the prothrombin. The former substance was recently shown by certain Italian investigators to undergo a diminution in concentration immediately after operation and subsequently to increase by the third or fourth day to nearly double the pre-operative value. This raised level is maintained for several days but figures are not available for more than the first seven when the concentration is still well above normal.

During the same post-operative period the activity of the prothrombin in the plasma is also enhanced. Shapero and his colleagues in 1942 followed the prothrombin levels daily in a series of cases following surgical operations, and demonstrated that the activity, after a preliminary decrease in the first few days, became markedly increased and reached a maximum about the tenth day. These findings led him to believe that hyperthrombinæmia may be used as a premonitory sign in thrombo-embolism. The desire to be able to foretell the onset of thrombosis is, naturally, very great and recently Mayes has suggested that the presence of a form of fibrinogen, fibrinogen B, which has been described by Lyons in Australia, if taken in conjunction with the prothrombin times and the patient's daily temperature, will give a reliable method of prognostication. Fibrinogen B is an intermediate substance produced in the conversion of fibrinogen into fibrin. Thrombin can be shown to consist of two components, neither of which will, alone, convert fibrinogen into fibrin. The thrombin component A reacts with fibrinogen to form the intermediate product fibrinogen B, which normally passes rapidly into the fibrin form. Mayes suggests that in the pre-thrombotic state the fibrinogen B fraction, which can very easily be demonstrated by the addition of a solution of naphthaquinone to citrate plasma, is greatly increased, and that this increase is pathognomonic of incipient thrombosis. While I am sure that the method of testing for the fibrinogen B is satisfactory, I am less convinced that the interpretation put upon its presence in the post-operative patient is correct. In repeating this work recently I have carried out the test every four days in patients following operation and delivery and in all the cases under observation have found that the fibrinogen B content of the plasma is increased. This rise is usually first apparent on the fifth to seventh day and is invariably recognized by the tenth day. Simultaneous prothrombin estimations on the same blood samples showed an increased activity even in the absence of any clinical or demonstrable thrombosis. It seems likely, therefore, that these chemical changes in the blood invariably occur in the post-traumatic period and give little indication of the likelihood of the onset of thrombosis. Finally, if the fibrinogen B and the prothrombin are neither true guides to the onset of thrombosis we are left with the third only of Mayes' criteria of prognostication—the temperature—and it is well known how easily urinary infections, chest complications and even lactation can cause sudden and unexpected rises in temperature. It seems that at present it is not possible to use such biochemical changes in the blood to predict with any degree of certainty the onset of thrombosis, and the only safe course is to rely upon careful clinical observation of the patient in the post-operative and puerperal periods.

But the chemical changes are not the only ones which occur in the blood at this time. The importance of the blood platelets has long been known and the part that they play in the initiation of thrombi in injured blood-vessels by their deposition over the traumatized area is well recognized. It was not until 1928, however, that Howell Evans and his colleagues in Liverpool showed that the blood contained a greatly increased number of these elements in patients after operations and parturition. They found that the increase in numbers might be as great as 100% or more and that it usually became apparent on the

He also wished to emphasize that the diagnosis of deafness in young children should remain within the province of the otologist. If he employed a technician to assist him the relationship should be the same as between radiologist and radiographer. They all knew that the best conducted radiological departments were those in which the radiographer was under constant supervision by the radiologist. In a highly critical technical procedure such as the Peep-Show it was of paramount importance that the work should be under the supervision of an experienced otologist.

Mr. C. Hamblen-Thomas said that this was a most useful piece of apparatus for the clinic. He wished they could get social workers at the clinics to assist in carrying out these tests and also in undertaking the follow-up of the children. It would be interesting to learn from Mr. Hallpike whether the hearing which remained showed signs of developing under training—whether the children's perception improved to any extent.

He added that some audiometricians were being trained at the Metropolitan Throat Hospital, but their future depended on the possibility of their employment. It was of no use training girls if there was no future for them. He agreed that the otologist must be in charge initially and primarily, but if there were trained girls available they would be of great help to the otologist.

Mr. Ian G. Robin said that he himself had not had such success with children under 5, but he thought the present instrument was most suitable for children between $3\frac{1}{2}$ and 5, and not suitable for most children of between 2 and 3. Here the Ewing technique played a very important part. He thought that the Peep-Show and the Ewing technique should have a place in all deafness clinics.

Mr. M. L. Formby said that it would be a great mistake for them to feel that this was something which could be tacked on as an adjunct to a busy ear, nose and throat department and left to technicians to carry out.

Mr. Hallpike agreed that it would be quite useless to have this kind of apparatus in a busy out-patient room, and to bring the child into such a place where other things were going on probably more interesting than the test. It was necessary to use the apparatus in a quiet room where there was nothing to distract the child's attention. Another practical point was that according to the terms of the Education Act of 1944 these children now become the responsibility of the Minister of Education *before* the age of 5. Therefore the diagnosis of deafness before the age of 5 was, for administrative reasons, more important than before. He agreed with Mr. Robin concerning the desirability of getting evidence of deafness before the age of 2. The Peep-Show was not suitable for this but it was, he thought, much the most effective means of obtaining a pure tone audiogram under the age of 6 years and such an audiogram did enable them better than anything else to meet the needs of Medical Officers of Health and others who demanded a clear-cut definition of the extent of the child's deafness.

Concerning finally the necessity for training technicians to assist otologists in these tests, Mr. Hallpike said that the technical procedure was designed to be fundamentally simple and capable of being understood and supervised by otologists everywhere. With that proviso it was not really necessary to create another branch of technical auxiliaries, because any intelligent assistant could do what was required.

dissected out, giving an accurate picture of the shape of the femoral vein as it passes over the pelvic brim. Casts were taken from a series of cases and in all instances the veins showed a marked antero-posterior flattening as they passed into the pelvis. This flattening is caused by the vein lying almost directly on the bone as it passes from the leg to reach the posterior wall of the pelvis, and is unrelated to the overlying femoral ligament. The effect is best likened to the kinking of a piece of rubber tubing drawn over the edge of a table. The average of 16 pairs of vein casts shows that the actual cross-sectional area of the vein at the mid-point of the bone of the pelvic brim is smaller than in the unflattened part 5 cm. above or 5 cm. below this point. The measurements are of the order of 28 sq. mm. at the point of maximal flattening against 36 and 39 sq. mm. at points 5 cm. below and above this point. It seems likely, therefore, both that an area of weakness occurs in any clot propagated beyond this point and that some degree of stagnation must occur below the constriction at the pelvic brim. The slowing of the blood and the nipping of the clot at this point may well play a part in the formation of small emboli which break from the unattached surface of the thrombus and may be the site of origin of repeated emboli of non-fatal nature in cases of femoral thrombosis.

The making of the venous casts brought to light a further feature in femoral anatomy which is of interest to obstetricians and gynecologists.

Vein casts taken from bodies in the supine position show that there is little distortion of the vessel except for the flattening, whereas those obtained after the legs had been flexed to correspond with "Fowler's position" were bent almost to a right angle at the pelvic brim. This additional distortion is caused by the vein being bound down firmly in the femoral triangle by fascia, and must cause some further obstruction to the free flow of blood at this point and below it. The stagnation so produced must facilitate the propagation of any thrombus forming in peripheral veins of the leg. The further elucidation of the problems of stagnation in the legs of patients confined to bed is an aspect of the study of thrombosis with which I am now concerned. You will have noticed that fig. 1 included a curve of the retardation of circulation time as measured from the leg to the carotid sinus in patients confined to bed. This slowing was progressively noticeable for the first eight or nine days when it became almost steady at the reduced velocity. These figures are not, however, altogether satisfactory, first because they do not continue after the 13th day of rest, and secondly because they are not a direct measurement of the time required for the blood to pass up the leg. Leg-carotid time includes the time the blood takes to pass through the venous side of the greater circulation, the whole of the lesser circulation and finally the arterial time from the left ventricle to the carotid sinus. It is assumed that the slowing recorded in these observations is dependent upon stagnation in the legs, since arm-carotid time shows no such change, but there is no proof that this is so and that the hold-up is not in some other part of the circulation. My colleagues and I are, therefore, attempting to measure the leg venous times directly by the use of the radio-active isotope of sodium, sodium₂₄. This is injected in the form of saline in the dorsal vein of the foot and the gamma emanations given off are recorded by a shielded Geiger counter placed over the femoral vein in the groin. The method appears to be satisfactory though at present we have made too few observations to be able to say either what the normal venous time is, or yet to assess the difficulties with which we may be faced. In one subject, however, we obtained an excellent example of the value of foot movement as a pumping mechanism to move stagnating blood along the veins of the leg. Na₂₄ was injected into the foot in a subject known to have severe varicose veins. By the end of a minute no radio-active sodium had reached the counter over the groin. At that moment the subject flexed his foot dorsally a little and within two seconds a shower of gamma rays were recorded at the femoral vein. It was evident that the blood had been held up in the dilated vessels of the leg and that the slight movement was sufficient to massage it along at a much increased rate. I am sure that the importance of supervised and graded exercises and early ambulation cannot be over-emphasized in prevention of thrombus formation in the post-operative and post-parturient patient and that these are the only satisfactory methods of overcoming the stagnation factor in the formation of post-operative thrombosis.

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fifth or sixth days, reaching a maximum about the tenth day and thereafter subsided to reach normality by the end of the third week. They also noted that the degree of increase in the platelet count was correlated with the severity of the operation, the more extensive the tissue damage, the greater the platelet response. In 1942, I was able to show that a further change in the platelets occurred concurrently with the increase in their numbers, namely that these blood elements become more adhesive. Observations made both on man after operations and delivery, and on experimental animals, proved that the increase in the stickiness of the platelets is maximal on about the tenth day and it appears that the new young cells which have entered the circulation in response to the stimulus of the trauma are responsible for this change in the adhesive properties of the platelets.

The correlation in time of both the chemical and the cytological changes of the blood, together with the incidence of thrombosis, are shown in fig. 1.

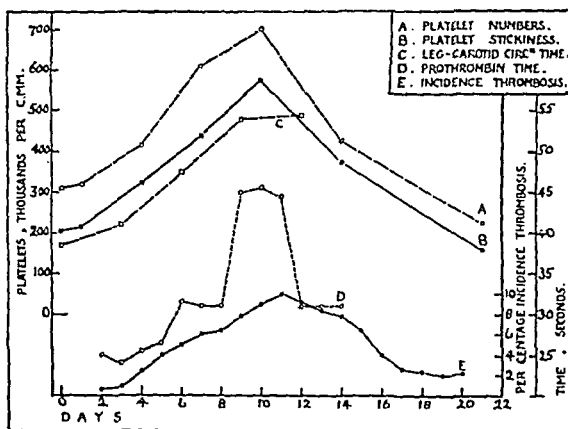


FIG. 1.—Incidence of venous thrombosis, blood changes and circulation times occurring in the post-operative period.

Here, too, is an incomplete curve (C) showing the changes in leg circulation times in a patient confined to bed, a factor in thrombosis about which I wish to speak presently. The closely parallel courses followed by these curves and their relation to the curve for the incidence of clinical thrombosis suggest that all the reactions are brought about by some common stimulus. In an attempt to elucidate what part of the surgical operation called forth the response, I performed some graded animal experiments in which rabbits underwent successive operations of increasing severity, from hæmorrhage and simple skin incision to splenectomy, and these observations confirmed that the extent of the rise in the platelet count is dependent upon the amount of damage to the tissues. It seems likely, therefore, that the stimulus to the bone-marrow results from the absorption of the products of tissue autolysis. This is further supported by the finding that a rise in the platelet count occurs after tissue damage other than that caused by cutting, and that the injection of necrotizing materials such as sterile silica dust or the exposure of the body to ultraviolet light are both followed by changes in the platelets similar to those occurring in surgical patients. Similarly, when tissue extracts or their products and especially the derivatives of nucleic acid are injected into animals, a platelet response is observed which corresponds to that in surgical cases.

I shall now pass to more mechanical aspects of venous circulation. The importance of venous stasis was first stressed by Virchow almost a century ago and he also pointed out that eddies in the regions of venous valves, side branches and alterations of calibre of the vessels might play a part in the development and propagation of intravenous clots. These views are still widely held, and though it is now recognized that the thrombotic process usually starts in the small plantar and calf veins, and not in the femoral vein itself, yet it is possible that the spread of the clot into the venous trunks may well be influenced by the physical features present in the large veins. Formerly anatomists believed that Poupart's ligament played an important part in thrombosis by causing a constriction of the veins at the level of the pelvic brim. But the ligament seems to me to be too lax and too anterior to exert any pressure upon the vein at this place. To test this, I tried running a plaster-of-Paris mixture, which maintained its size unaltered on setting, into the veins of cadavers, from the mid-thigh region to the common iliac. The vein was first carefully washed out with saline and the plaster was then introduced at about normal venous pressure. When it was flowing freely from the lower to the upper cannula, both ends were clamped simultaneously so that the pressure in the vein was maintained. After the plaster had set thoroughly, the cast was

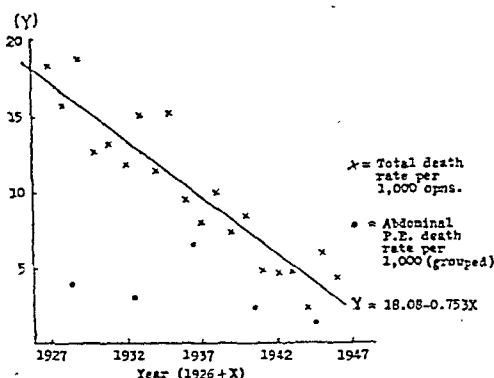


FIG. 1.—Graphic comparison of total death-rate per 1,000 operations and post-abdominal pulmonary embolism death-rate per 1,000, the latter grouped by four-year periods.

TABLE I.—ANALYSIS OF OPERATIONS AND DEATHS FROM PULMONARY EMBOLISM, AND OTHER CAUSES, FOR TWENTY YEARS, 1927–1946

Year	Total operations	Total deaths	Total deaths from P.E.	Abdominal operations	P.E. deaths	Non-abdominal operations	P.E. deaths
1927	1,470	27	4	795	3	675	1
1928	1,456	23	3	707	2	749	1
1929	1,535	29	5	721	5	814	0
1930	1,577	20	3	766	2	811	1
1931	1,511	20	4	638	3	873	1
1932	1,512	18	4	662	3	850	1
1933	1,395	21	2	612	2	783	0
1934	1,586	18	1	629	0	957	1
1935	1,586	24	4	604	4	982	0
1936	1,677	16	8	649	8	1,028	0
1937	1,749	14	0	676	0	1,073	0
1938	1,295	13	4	456	4	839	0
1939	1,512	11	4	508	2	1,004	2
1940	1,178	10	3	409	2	769	1
1941	1,213	6	0	375	0	838	0
1942	1,483	7	1	466	0	1,017	1
1943	1,892	9	2	546	2	1,346	0
1944	1,248	3	0	451	0	797	0
1945	1,675	10	1	486	0	1,189	1
1946	2,091	9	2	592	1	1,499	1

TABLE II.—DEATHS FROM PULMONARY EMBOLISM AFTER ABDOMINAL OPERATIONS. EXPECTED DEATHS, ASSUMING A UNIFORM DEATH-RATE OF 3·660 PER 1,000 THROUGHOUT, COMPARED WITH ACTUAL DEATHS

Years	Expected	Actual
1–2	5·497	5
3–4	5·442	7
5–7	6·998	8
8–10	6·888	12
11–13	6·002	6
14–16	4·575	2
17–20	7·595	3
	42·997	43

The analysis of χ^2 is :

	Degrees of freedom	χ^2	P
Discrepancy between 1st and 2nd ten-year periods	1	4·92	0·025
Residual discrepancies	5	3·77	0·5–0·7
Total	6	8·69	

Dr. Magnus Haines: *Pathology of post-operative thrombosis.*—It is intended to confine these remarks to the morbid anatomy of non-septic thrombosis. Thrombosis, when recognized, causes the surgeon anxiety on two scores, (1) the patient's convalescence must be prolonged, and (2) the patient may die as a result of dislodgment of a thrombus or a portion of it. It is commonly recognized that the sites for thrombosis are the pelvic veins, the common, superficial and deep femoral veins. During the past decade interest has been revived in following the dissection of the leg veins to *below* the knee. The results have been (1) that in post-operative cases the oldest part of the clot has been found in the veins of the deep calf muscles, and in the popliteal, and (2) thrombosis in the same location has been noted in up to 25–50% of patients, mostly over 40 years of age, who died of a variety of conditions of no surgical interest, but who had been bedridden by their illness. These investigations have not, however, helped in any way to establish an answer to the question "how soon after an operation may thrombosis occur?" But at the same time it is obvious that thrombosis may be present even before operation in patients who have been in bed some time. A more detailed account has been given by Short.

Clinically it is important to remember that (1) Thrombosis is often symptomless and without physical signs. (2) Time of onset is variable, not "ten to twenty-one days after the operation". (3) Most of the patients are over 40 years.

Convalescence may be prolonged because of the thrombosis or because of embolism. It is held by some that nearly all fatal embolisms occur in cases of unsuspected thrombosis. Embolism commonly occurs in one of two clinical forms, the second sometimes following the first. In the first we have embolism, usually pulmonary, leading to small infarcts. Pulmonary infarction has a characteristic clinical picture, but I would stress that it may be silent in onset or the symptoms and signs, often atypical, may be misinterpreted, e.g. as pneumonia, basal collapse, paroxysmal tachycardia. The mechanism by which the thrombus becomes separated is not yet clear. In some cases, small pieces of the proximal end become emboli while in others the embolus is 45 to 55 cm. long. Undue friability of the clot may account for its fragmentation. It is probable that the "long embolus" results from some agent which breaks down the clot's anchorage to the endothelium. It is finally separated by intravascular friction associated with increased blood flow.

I do not propose to deal with the prevention of thrombosis or its treatment. There can be little doubt that solutions of the many problems will be found, as indicated by Short (1947, *Proc. R. Soc. Med.*, 40, 195), in changes taking place in the plasma, and in the corpuscular elements of the blood, particularly platelets. Here I would call for a much more careful record-keeping by our clinical colleagues, with publications, of the incidence of post-operative thrombosis and non-fatal embolisms. As pathologists we have no difficulty about recording the fatal cases.

In order to gain some idea of the incidence of fatal pulmonary embolism we have reviewed the operations performed at Chelsea Hospital for Women from 1927 to 1946 inclusive. There were 55 cases of fatal pulmonary embolism in over 30,000 operations performed. Abdominal operations numbered 11,748 with 43 fatal pulmonary embolisms. "All other operations" showed 12 fatal embolisms. The twenty years can be divided equally and it is found that just over 15,000 operations were done in each period. Furthermore, a new regime of physiotherapy was operating during the second ten years. At first sight, the figures indicated gratifying results in the latter group. But it became apparent that other factors required consideration.

Thus from Table I it is seen that the total deaths per 1,000 operations have fallen steadily, on the average, during the whole twenty-year period, although they clearly cannot continue to fall at the same rate. If Y is the death-rate per 1,000 and X is the year, coded so that 1927 = 1, 1928 = 2... 1946 = 20:

$$Y = 18.08 - 0.753 X \dots \text{approx.}$$

This line is a very good fit to the data (*see* fig. 1), its slope is more than 10 times the standard error and is thus highly significant statistically. The departures of the observed death-rates from this line are no more than is to be expected by chance ($\chi^2_{[15]} = 11.69$, $P = 0.80$ to 0.90) and a curve does not fit the data significantly better than this straight line.

On the other hand deaths due to pulmonary embolism are not so clearly dependent on time as are the total deaths. During the first ten years there is no indication of a changing death-rate. Such changes as occur in the second ten years relate only to abdominal operations. In order to examine the likelihood that the abdominal pulmonary embolism fatality rate during the second ten-year period differed from that during the first, a χ^2 test was made, grouping the data so as to obtain expected numbers of not less than about 5 on the hypothesis that a uniform death-rate of 3.660 per 1,000 held throughout the twenty years. On this hypothesis, the expected and actual deaths are shown in Table II.

(1) Pulmonary embolism.—The majority of first pulmonary embolisms are small ones and frequently are diagnosed as pleurisy and put down to post-operative chill from sweating, cold corridors and so on; the one small tell-tale disc of blood-stained sputum produced twenty-four or forty-eight hours after the pain is not noticed, or if noticed, not reported. It would be safe to generalize and state that every case of stitch-like pain in the ribs after an operation is an embolism and, furthermore, a warning of others to come and a 30% chance of fatality. A second important generalization is that the embolism originates in the posterior tibial veins, and even if not clinically evident, the ligation of both superficial femoral veins should be carried out at once; this done one need have no further anxiety on the score of embolism. Heparin and dicoumarol therapy is also employed after the ligatures to make assurance doubly sure. It often happens that after a bilateral ligation the affected leg, not apparent clinically, generally the left, will disclose itself by swelling up while the other shows no change of any kind; the amount of this swelling is greatly reduced by anticoagulant therapy possibly combined with lumbar ganglionic block.

(2) Thrombosis of varicose veins after operation is very worrying. These veins themselves never manufacture emboli, but the thrombus may extend to the saphenous or popliteal opening and involve the deep veins, or—more important—the post-tibial veins may also share in the general insidious tendency to clot and do so, as they often do, without producing any clinical signs. On the whole I think it safest to ligate the common femoral veins above the saphenous openings in these cases.

(3) Thrombosis of normal superficial veins either spontaneously or following venoclysis. In these cases the legs should both be carefully examined for deep thrombosis, and if this is the only lesion ligation of the common femoral vein should be done on the same side above the saphenous opening. It is best to avoid the leg veins entirely for venoclysis and only resort to them in dire necessity when the arm veins are exhausted.

(4) Phlebothrombosis of the posterior tibial veins is a very insidious condition and is frequently missed. The pain is not great and is not reported by the patient who thinks it is a "muscular strain", and frequently there is no pain at all. The condition will only be discovered by routine examination of the lower calves for tenderness and pain in the same region on dorsiflexion of the foot (Homans' sign). The condition sometimes produces a steadily rising pulse-rate (Mahler's sign) and a mild pyrexia. Once discovered the condition must be regarded as urgent and dangerous and ligation of the superficial femoral vein made at its junction with the deep vein on the affected side. The usual anticoagulant therapy follows the operation.

(5) Massive femoral thrombosis thrusts itself on the attention, but it cannot be too strongly stressed that it is often preceded by the less obvious conditions above (1, 2, 3 and 4) and if steps had been taken in time, this final dénouement would not arrive and much trouble avoided for all. Phlegmasia alba dolens in full flower is an awesome sight. The leg, soapy-white or cadaveric blue, ice-cold from sweat and blown up as tight as a football, produces great systemic disturbance if development is rapid by the great abstraction of fluid from the rest of the body. When both legs are inflated simultaneously the abstraction of fluid may be so great as to produce a fatal outcome. On two occasions I have been able by administration of intravenous saline to snatch a moribund patient from the grave; in one case the collapse was thought to be due to pulmonary embolus and in the other to a cardiac infarct. A litre of intravenous normal saline was enough to make the diagnosis clear. In phlegmasia alba dolens it was customary in other days to stand helplessly by, give morphia to the immobilized patient and watch the condition progress, frequently spread to the other leg and finally slowly defervesce; after six to twenty-four weeks of extra bed the patient would get up crippled for life. Thanks to the genius of Leriche this is no more; he pointed out that the leg was cold and icy and it was easy to alter that, and that done, other benefits might accrue. The lumbar ganglia are injected with novocain immediately the condition is manifest, the leg warms, arterial and venous spasms disappear, the blood flows freely, the vicious circle is ended and the swelling starts to go down; no more morphia is needed and generally within a week the patient, with appropriate support for the leg, is out of bed. Most important of all, the permanent damage is lessened, and we can hope that twelve years later there will be a reduction if not an absence of the hitherto inevitable pigmentation, ulceration, eczema, callous œdema and recurrent phlebitis which we see at present.

For many years tentative efforts in which I have joined from time to time have been made to extract the clots from the femoral veins so as to diminish the permanent effects. Phlebography as practised by Dos Santos promises to put this on a more rational basis, and the extent of the clot can be accurately defined and a suitable operation planned with good prospects of success.

(6) Iliac thrombosis is of special interest to the gynæcological surgeon. There is no doubt that the iliac vein close to the operation area is the initial starting-point in certain cases of femoral thrombosis but in only relatively few cases. The more usual thing is for it to start

Thus, there is a statistically significant difference between the fatality rates for the two ten-year periods, but no evidence of further discrepancy. The chance is approximately 40 to 1 that the death-rate fell in the second ten-year period as compared with the first, and the best estimate of this fall is from 4.72 per 1,000 operations to 2.22 per 1,000. It should be noted that this is very much the same as the general fall in all deaths of from 14.1 per 1,000 in the first period to 6.0 per 1,000 in the second.

It is hoped that when the next ten-year survey is reported, a still greater reduction in fatality rate will have been achieved as the result of efficient use of anticoagulants.

Mr. A. Dickson Wright: Post-operative complications have one by one been circumvented by improvements in the performance of the operation and the administration of the anæsthetic combined with more rational treatment before and after the operation. In addition, these complications themselves, if they should develop in spite of all precautions, can be treated much better with modern agents. The occurrence of venous clotting after operations and childbirth is an accepted fact although some are inclined to minimize it and say that it never occurs in their personal practices. This attitude is not correct or fair to patients, the condition is prevalent enough to be taken seriously, it is dangerous to life and will, if recovered from, leave disabilities and miseries for the rest of the patient's lifetime. There is a certain reluctance to take precautions against the condition because it is said to be so rare, and when the condition has developed in spite of its rarity, precautions are not taken against embolism because that in its turn is stated to be rare also, and finally all the resources of treatment are not employed to ameliorate the condition. The sequelæ are remote, frequently not developing seriously till twelve years later, and their inevitability is not realized by all. A greater feeling of responsibility to prevent post-operative thrombosis should be evident, and when unfortunately it does occur, embolism must be prevented and everything possible done to reduce the severity of the local condition so as to leave the patient with as little crippling as possible.

Earlier speakers have stressed the post-operative blood changes which conduce to intra-venous clottings and to these I would like to add one more, viz. the increased sedimentation of the blood cells which leads to more concentrated blood and increased blood viscosity in the lower parts of the body, especially if the patient is sitting in bed.

Apart from the hæmatological factors there are certain mechanical factors which play a part. The Fowler's position causes venous stagnation in the legs and pelvis and should be abandoned; it has been now shown to be of little advantage in peritonitis for which it was invented, and it could safely be allowed to slip into the limbo of the past except in very special circumstances. Patients like to sit up in the daytime, but they should get down at night and for their afternoon siesta and be encouraged in every way to sleep upon the side. Early ambulation is becoming rapidly accepted, and expected and enjoyed by the public and the nursing profession (the bed-pan may become soon a museum piece). Early ambulation is not possible with catgut suturing of the abdominal parietes and interrupted silk stitches or a continuous steel wire stitch will have to be used. This means that operations will take a little longer but the patients will get well quicker. In addition the operation itself should be gently done and blood must not be shed needlessly, because the less the trauma and the less the blood loss the less the thrombosis incidence. Starvation before or after the operation must be reduced to the minimum, and purgation should be restrained. It is a bad custom to put the patient to bed for several days before operation. This is sometimes done to get the patient relaxed and accustomed to his new surroundings or more often to suit the surgeon's convenience or operating days. A very dangerous type of case is the one handed over by the physician after a long sojourn in bed for medical treatment which, when it fails, leads to operation. With early ambulation, bed exercises have lost their importance, but if the patient does not get up the day after the operation, then he should do some deep breathing and muscle twitching before he does.

There is one type of case requiring special consideration and that is the thrombophilic individual with a long history of thrombosis on the slightest provocation who now has to face unavoidable operation. Such patients must never have pyelographies, cholecystographies or anæsthetics by the intravenous route. At the time of operation it is well to tie the superficial femoral veins and for three weeks or even longer after the operation to keep the patients under heparin and dicoumarol therapy. A bad family history of thrombosis or embolism would also justify these measures, as would splenectomy with its bad record for thrombosis and embolism. If a fatal embolism occurs in such a case, with all concerned fully aware of the danger, it will soon be hard to exculpate the surgeon in the present state of knowledge if he has not taken the precautions mentioned.

After operation there are many different manifestations of thrombosis, and it is essential to be on the look-out for them so that prompt measures can be taken. The various situations which may confront the surgeon are as follows:

for post-operative cases. Admittedly, some surgeons get their patients up very early, but the patients do not like it. My practice is still rather conservative, both obstetric and gynaecological patients not being allowed up until the tenth day, or later.

With reference to the value of graduated post-operative exercises conducted under the direction of the ward sister and sometimes to the accompaniment of music, I should like to quote the very striking summary of Sir William Fletcher Shaw's article in the *Journal of Obstetrics and Gynaecology of the British Empire*, 45, No. 3, 451. "In two institutions in wards under the care of the same gynaecologist, admitting the same type of patient, with the same pre-operative and post-operative treatment—except that in one systematic graduated post-operative exercises were given and not in the other—this gynaecologist performed 1,635 consecutive operations in the hospital with graduated exercises with an incidence of fatal pulmonary embolism of 0.06%." In the other hospital without graduated exercises the same gynaecologist performed 3,618 operations with an incidence of fatal pulmonary embolism of 0.304%, a percentage incidence five times as great as in the other group.

To turn now to some of the more modern treatments. It is well recognized that even cases of sudden and severe pulmonary embolus can now be saved by using large doses of heparin immediately. It is probable that we have been using far too small a dose in this country. We have been using such quantities as 5,000 units, in reality this is only 50 mg. and quite inadequate.

There is confusion nowadays because the dose may be referred to as milligrams or units. All that need be remembered is that 1 mg. of pure Toronto heparin corresponds to 100 units. Now, the usual preparation available is Liquemin Roche, which is put up in 5 c.c. ampoules, containing a total of 50 mg. To give a dose adequate for a case of pulmonary embolus would thus mean giving 2½ ampoules (125 mg. 12,500 units) immediately and 2 ampoules at five-hourly intervals. To avoid waking a patient it is wise to make the last dose at night 2½ ampoules, i.e. 125 mg.

The net cost to a hospital of one ampoule is 8s. 4d. The cost of 1 dose therefore averages about £1 and the daily cost in the region of £5 to a hospital. We private practitioners would pay much more. The concentrated solution which used to contain 5,000 units per c.c. unfortunately appears to be unobtainable at the moment. In any event, the cost of the treatment will be about the same, for 1 ampoule of this concentrated solution used to cost £2 net to hospitals. Heparin is always given intravenously and intermittent injections seem preferable to continuous dilute transfusion. It is merely a matter of drawing the contents of 2 or 2½ Liquemin ampoules into a 20 c.c. syringe and injecting it slowly, intravenously.

Temparin is another available and cheaper anticoagulant but it has a time-lag of forty-eight hours or thereabouts. So heparin *must* be given for the first two days. At the same time, temparin is started and it can be expected to take over anticoagulant duties in about two days' time. The initial dose should be 300 mg. 200 mg. is given on the second and third days. No more temparin is given until the prothrombin time is estimated. This is usually done on the fifth day and if a correct increase has taken place, maintenance doses of approximately 100 mg. daily are given. Temparin is always given by the mouth. No advantage is gained by giving it intravenously or intramuscularly. But its effect must be checked by repeated estimations of the prothrombin time. It is most remarkable to observe the differences of response to temparin in different patients.

The exact mode of action of heparin appears to be unknown. The action of temparin has been aptly described as that of a toxic narcotic to the liver cells. It thus prevents the formation of prothrombin. In estimating the prothrombin time several methods are used and it is necessary that the report should show the normal finding and the finding in the tested blood. It is desired to rather more than double the prothrombin time. If 25 be said to be the normal, one would want to find a figure of 55 to 60. If this is achieved the blood prothrombin is down by about 80%.

Embolectomy and pulmonary embolectomy are heroic surgical adventures!

Ligature of the femoral vein on both sides following the discovery of thrombosis in the veins of one or both calves seems to me just a wild piece of blood-and-iron surgery. Admittedly the ligation is done distal to the profunda femoris but even so it is, I think, an example of exalting technique at the expense of judgment even when one appreciates the horror of a fatal pulmonary embolus that occasionally will follow the development of venous thrombosis starting in the calf. This is, after all, a rare happening and its rarity to my mind condemns this treatment and makes ridiculous the practice of one American who ties both femoral veins as a preliminary to abdominal section.

Paravertebral sympathetic block, on the other hand, is a treatment of which I speak with almost unqualified praise. When I first read up the work of Leriche, Ochsner, De Bakey and others I got Mr. Dickson Wright to do a sympathetic block on two patients, one a white leg in pregnancy and the other a similar condition in the puerperium. The relief was

in the posterior tibial veins, as with all abdominal operations and spread up the femoral veins to the iliacs which with their traumatized branches readily join in, and sometimes the lower end of the vena cava and the opposite common iliac are affected. The condition is treated by lumbar ganglionic block, inferior vena cava ligation if pulmonary embolism occurs and possibly in the future by phlebography and thrombectomy. Ligation of the inferior vena cava is also indicated whenever pulmonary embolism occurs after femoral ligation, which is very rarely. It seems opportune to repeat that heparin and dicoumarol therapy is employed in all these post-operative thromboses, and the dosage is 12,500 units of heparin intravenously at 8 a.m., 10,000 at 12 noon, 4 and 8 p.m. and 12,500 at midnight for two days and then the dicoumarol, which has been administered simultaneously by mouth for these two days, takes effect. The dose is 300 mg. the first day, 200 on second and third days and subsequent doses to keep the prothrombin time 220% of normal. The heparin for the first two days should keep the clotting time at twenty minutes. Some surgeons fear dicoumarol and use heparin for the whole of the dangerous period, but the administration is expensive and troublesome for long periods.

Although the legs are the site of nearly all post-operative thromboses, certain cerebral, cardiac, retinal and intestinal thromboses occur at the same intervals after operation as do the leg thromboses, and are really post-operative complications. They are too rare to be treated in anticipation but if occurring after a leg thrombosis, some regrets would be felt if anticoagulants had not been used. Thrombosis of the arm veins following pentothal or venoclysis is annoying rather than dangerous and requires no treatment. Arterial thrombosis after operation occurs in severe degrees of thrombophilia and one such patient who, against my advice, had ligation of varicose veins carried out, suffered the loss of an arm and a leg from this cause. Patients with fibrillation are more prone to form auricular clots after operation and embolize to the systemic arteries. This is especially common after operations for thyrotoxicosis.

The price of freedom from post-operative thrombosis is unrelaxing vigilance. The first signs must be watched for in the proper place, below the calves, under the ribs and on the temperature chart, and there must be no hesitation in applying the proper treatment, drastic as it may seem. It is a well-known fact that the relatives of the person deceased from embolism are prone to be very vindictive, very often without reasonable grounds, but, from now on, they will show even less mercy and may even exact retributions for precautions left untaken.

Mr. Leslie Williams: Though the subject under discussion is post-operative thrombosis much that is said must apply equally to puerperal thrombosis. We gynaecologists have had a sinister reputation in the past, for having our work complicated by venous thrombosis. I do not think that thrombosis nowadays follows gynaecological operating any more than it does general surgical work. Nevertheless, we all do meet cases from time to time and we are still enthusiastic to discuss prophylactic measures and all methods of treatment.

My interest in venous thrombosis was first aroused in the time of the Isolation Block of Queen Charlotte's Hospital. There a few of us, at times, tried to prevent spread of blood-stream infection by ligating veins along which we judged infected clot to be spreading. Sometimes we tied the ovarian vein on one or other side and sometimes the two or three veins which return the blood from the pelvic organs to the iliac trunk. This treatment has become more or less obsolete since the advent of chemotherapy and we are now more interested in thrombosis in veins from the legs.

The whole basis of the modern ideas of treatment of this form of post-operative thrombosis is the knowledge that these thrombi practically always start peripherally in the small deep veins in the calf and almost never in the iliac veins.

At first these thromboses are more or less silent and perhaps at times diagnosable only by intravenous injection of some radiopaque substance and subsequent X-rays. This method has never gained much favour in this country and many regard it as dangerous. In any event it may be unnecessary since I gather from Mr. Dickson Wright that daily palpation of the calf muscles will elicit tenderness in the very early stages of thrombosis and that pain on dorsiflexion of the foot is an equally early and valuable sign.

More commonly we have to deal with an established thrombosis which is recognized by pain as well as early tenderness in the calf, or by the development of "white leg". Sometimes the sudden appearance of pulmonary embolus is the first appreciable sign.

PROPHYLAXIS

In the attempt to minimize the dangers of thrombus formation, the early employment of massage, active and passive movements, &c., is now almost universal. Early rising after labour, the patient perhaps being allowed up on the second or third day, has quite a number of advocates. It has many points to recommend it but the idea is not so popular

leg has occurred. Treatment with anticoagulants does, in my experience, prevent the spread of the thrombosis from the calf to the thigh.

A combination of heparin and dicoumarol is used. Heparin is given by intravenous drip transfusion at a rate of 1,000 to 1,500 international units per hour for forty-eight to seventy-two hours. Dicoumarol is commenced at the same time, as its anticoagulant effect does not occur for two to three days. 300 mg. are given by mouth on the first day and 200 mg. on the second day. Estimations of the prothrombin index are performed daily after the first forty-eight hours. The aim is to lower the prothrombin index to between 40 and 60% of normal, and dicoumarol (usually 100 mg.) is given daily until this level is attained. When the patient is fully ambulant, usually after one week, the dicoumarol is omitted. In the puerperal cases an average of 60,000 I.U. of heparin were given over fifty hours and an average of 1,000 mg. of dicoumarol were given over 6.5 days.

Active exercises are commenced after forty-eight hours, the patient being encouraged to get up as soon as possible. Pain in the leg usually disappears within a few days, so that the patient is anxious to get out of bed.

TOXIC REACTION

There is a certain risk of hæmorrhage occurring from the use of dicoumarol and because of this, accurate estimations of the prothrombin index must be performed daily. In the present series of 11 puerperal deep thromboses only 2 developed a red lochia for a few days, and one of these patients also had a small epistaxis. The incidence of hæmorrhage in all cases treated so far (medical, surgical and obstetric) is about 25%, including minor hæmorrhages. In only one patient was the hæmorrhage serious, however, and she responded well to intravenous vitamin K (150 mg.) and a fresh blood transfusion. With more careful control the incidence of hæmorrhage should be reduced in future.

RESULTS

During the past year 11 cases of puerperal deep thrombosis have been treated and my thanks are due to Mr. J. S. MacVine and Miss M. A. M. Bigby under whose care they were confined. Similar results have also been obtained in the surgical cases. Owing to the very satisfactory results, it did not seem justifiable to use alternate cases as controls. Instead the records of women confined between 1942 and 1946 were surveyed by Mr. R. A. Kinch who found that 16 cases of definite deep thrombosis had occurred during these years. They had all been treated conservatively with complete immobilization. These were compared with the cases treated with anticoagulants for: (1) Length of stay in hospital; (2) length of confinement to bed after the thrombosis had developed.

	Conservative treatment 1942-1946	Anticoagulant treatment 1946-1947
Cases of deep thromboses ..	16	11
Average length of stay in hospital (days)	68	22
(Range)	(26-106)	(10-32)
Average length of confinement to bed after thrombosis (days) ..	45	8
(Range)	(12-100)	(3-12)

The results have also been compared as regards the incidence of pulmonary embolism and as regards the relapse rate of the thrombosis while the patient is in hospital.

	Conservative treatment	Anticoagulant treatment
	16 cases	11 cases
Pulmonary embolism ..	3 (1 fatal)	-
Relapse of thrombosis ..	4	1

It is noticeable, however, that relatively more cases occurred during the past year than in the previous four years as is shown in the following table.

	Incidence of thrombosis 1942-1946	1946-1947
Deliveries	7,147	1,831
Thromboses	16	11
Incidence	0.22%	0.6%

really dramatic. In any successful case the improvement in the general condition of the patient and the local condition of the affected limb is quite striking. The ill, pain-wracked and miserable patient is, within a matter of twenty-four hours, quite a different person. The cold white painful limb is comparatively warm and much less painful, sometimes within half an hour.

It is curious that in these cases of massive thrombosis we have the paradox of a cold swollen limb in a patient whose skin elsewhere is hot; and though the lesion is venous the symptoms and signs are the result of arterial spasm. This spasm is the cause of that damage which makes sympathetic block such a valuable treatment; for by interrupting the reflex, the arterial spasm is relieved, vasodilatation occurs and relief is gained. The same break in the reflex arc can be produced by a spinal anæsthetic, or by a high extradural anæsthetic. But I am advised that the effects produced by these methods may be much more short-lived than those produced by sympathetic block. Once relief of vasospasm is produced by this latter method, the effects appear to be permanent.

The operation itself is far from pleasant. A needle prodding its way along the sides of a vertebral body can be quite offensively painful. And indeed patients dislike the treatment intensely. But once some of the anæsthetic solution has been injected the rest of the operation becomes progressively less painful. Remember, however, that four or sometimes five places are injected.

Sometimes the needle point enters the aorta or the vena cava! It is therefore essential to withdraw the plunger each time before any novocain is injected to be sure of avoiding injection directly into the blood stream.

A great deal of novocain is used—up to 1 gramme. So an occasional toxic effect may be expected. A handy dose of pentothal ready for intravenous injection might come in useful as it would at once abolish novocain convulsions.

Lastly, the method must be applied early—as soon as thrombosis can be diagnosed. It may occasionally give relief in a case of established white leg of several days' duration. But if the treatment is applied early, and if the novocain solution is correctly placed in the neighbourhood of the sympathetic chain by perhaps two or three of the injections, one can be really confident of securing a most remarkable improvement. I highly commend this treatment.

To recapitulate: I strongly recommend immediate intravenous heparin treatment and immediate dicoumarol (temparin) oral treatment together with paravertebral sympathetic block for any patient in whom venous thrombosis in the deep veins of the leg is diagnosed. But I will not, as yet, have anything to do with ligature of the femoral veins, to say nothing of caval ligation.

Dr. K. P. Ball: I should like to describe briefly the treatment of venous thrombosis and pulmonary embolism with the anticoagulant drugs heparin and dicoumarol, which has been in use for the past year at Central Middlesex County Hospital. The 46 cases treated have been drawn from all departments of the hospital—medical, surgical and obstetric—but I shall pay special attention to the cases of thrombosis occurring during the puerperium.

CASES TREATED WITH ANTICOAGULANTS

Medical	24
Surgical (7)	
Appendicectomy	2
Myomectomy	1
Hysterectomy	1
Colpoperineorrhaphy	1
Herniorrhaphy	1
Ligature and injection of varicose veins ..	1
Obstetric (15)	
Puerperal	12
Pregnancy	1
Post-abortion	2
Total	46

Special stress is laid on the prophylaxis of venous thrombosis by active leg exercises for all patients confined to bed; particularly following childbirth. The early diagnosis of venous thrombosis is considered to be of paramount importance. A careful watch is kept for such early symptoms and signs as pain in the calf which is often worse at night, deep tenderness in the calf muscles, pain in the calf on dorsiflexion of the foot (a sign first described by Homans) and inexplicable temperatures. Following early diagnosis, treatment can be commenced when the thrombosis is limited to the calf and before the fully developed white

employed only for operations of very short duration, particularly those in which there was no great effusion of blood. Its effect on the parturient uterus was quite unknown. When, therefore, Simpson resolved to use ether in midwifery practice—which he did after a visit to his one-time colleague, Liston, the first man in this country to use anæsthesia in surgery—he searched for a case in which a short obstetric operation would be clearly required.

Before long such a case was forthcoming. The patient was a woman with a grossly contracted pelvis; a previous labour had lasted four days and had ended in craniotomy followed by one hour's traction with the crotchet. Contrary to instructions, the woman had not reported the occurrence of this second pregnancy till she had almost reached term, thus precluding treatment by the induction of premature labour. When at length labour-pains became established, Simpson, assisted by Dr. Keith, Dr. Figg and Dr. Zeigler, induced anæsthesia; this successfully accomplished, Simpson proceeded to turn the fœtus by internal version and to extract it in the breech position. Unfortunately, although the infant gasped a few times after birth, full respiration could not be established. It may interest present-day obstetricians to know that the conjugate diameter of this woman's pelvis was estimated to measure no more than $2\frac{1}{2}$ in. and that the baby when born was 8 lb. in weight! The mother, it is recorded, was amazed to find that the long-dreaded delivery had been accomplished while she slept. She made an excellent recovery and was up and dressed on the fifth day.

Pleased, and indeed elated, as Simpson was by the splendid results obtained with sulphuric ether in midwifery, he soon became convinced that other and even better agents might be forthcoming. Accordingly, with his assistants George Skene Keith and James Matthews Duncan, he began a systematic search in which those three workers tested on themselves the effects of inhaling the vapours of a great variety of chemical substances. On November 4, 1847, after much patient and dangerous work the anæsthetic properties of chloroform were discovered—a far better and stronger drug, they believed, than ether. Five days later, this new substance was successfully used in midwifery, and, on the following day, in surgical operations conducted by Professor Miller. Within eleven days Simpson was able to record its administration on no less than 50 occasions. The results were presented for publication on November 15, 1847.

Thus we find that, during this month of November, one hundred years ago, the news of the moment in every medical centre of Britain, of Europe generally, and of America, was the extension of the use of anæsthesia to midwifery practice; and particularly the use of the new drug chloroform—a drug supposedly superior to ether because of the rapidity of its action, the absence of unpleasant choking effects, and the ease and convenience of its administration.

James Young Simpson was the son of a none-too-prosperous baker in the village of Bathgate, eighteen miles from Edinburgh. When he arrived in the University to study Greek and Philosophy he was, by his own statement, "very, very young; very solitary, very poor and most friendless". Seven years later he had graduated as Doctor of Medicine; after eight



Sir James Young Simpson.
(From a portrait by Norman Macbeth,
R.S.A.)

more years he was appointed, at the age of 28, to the University Chair of Midwifery. Soon, his remarkable powers as clinician, investigator, writer and teacher had made his name one of the best known in the whole medical world. Among earlier honours bestowed on him was his appointment as Physician in Scotland to Her Majesty the Queen. By strange chance, the letter announcing this honour was on its way to him at the very moment when he was administering the first anæsthetic ever to be given to a woman in labour. In a private note written shortly afterwards to his brother, Simpson remarked: "Flattery from the Queen is perhaps *not* common flattery, but I am far less interested in it than in having delivered a woman this week *without* any pain while inhaling sulphuric ether. I can think of nought else."

Simpson's ability for sustained work was amazing. His day started in the early hours of the morning—sometimes as early as 4 a.m.—when he dealt with correspondence and prepared his lecture for the day.

Simpson's interests ranged over the whole field of medicine, and many of our everyday procedures in gynaecology were first described, or perfected by him. He was the first to give an adequate description of the method of bimanual palpation. By introducing the

It is suggested that the difference in the incidence of thrombosis in the two series is due to too few cases being diagnosed from 1942-1946, as the incidence during the past year of 0.6% is itself lower than in many series. Consequently, it must be admitted that the more severe cases from 1942-1946 are being compared with all cases during the past year. But this could only account for a small part of the very striking difference between the two series. Furthermore, the present results showing a reduction of the recumbent period from forty-five days to eight days are confirmed by Bauer (1946). He found that the recumbent period due to the thrombosis had been reduced from forty days in 264 cases with conservative treatment, to 4.7 days in 209 cases using heparin. Zilliacus (1946) found that the stay in bed was reduced from 35.1 days in 214 cases treated conservatively to between 8.1 and 10.5 days in 103 cases, using heparin and dicoumarol together.

In conclusion, I submit that the present treatment shortens the stay in hospital of these patients to about three weeks and the stay in bed to about one week. It has reduced the risk of pulmonary embolism and is likely to diminish greatly the percentage of disabling after-effects which so often cause such distress to these people in later years.

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Mr. V. B. Green-Armytage said that the work of Dr. Payling Wright was of sterling importance in the understanding of this condition, but what he would like to ask was why embolism and thrombosis were so rare following pelvic operations from below. This was a fact that had been observed by many American writers and despite the tissue trauma which must follow vaginal hysterectomy, or Fothergill's operation, it was a remarkable fact that complications were very rare. In a series of 4,000 vaginal operations the speaker himself had never seen a case of embolism or thrombosis, though following myomectomy or ordinary laparotomy for gynaecological lesions it was found to occur in one in every 480 cases.

For many years the speaker had never employed the Fowler's position for any kind of gynaecological operation and had made it a constant rule that patients should get out of bed on the third or fourth day. There was no reason why the trauma of vaginal operations should be exempt from thrombosis, whereas that in the closed cavity of the abdomen was so far from exempt.

[November 21, 1947]

A Note on the Centenary of the Use of Anæsthesia in Obstetric Practice by J. Y. Simpson

By Professor J. CHASSAR MOIR, F.R.C.O.G., F.R.C.S.Ed.

It is altogether fitting that we in this Section of the Royal Society of Medicine, direct descendants of the oldest Obstetric Society in Britain, should mark and honour the centenary of the event that has probably been the greatest single landmark in the evolution of our specialty. On January 19, 1847, anæsthesia was used for the first time in childbirth. James Young Simpson of Edinburgh was the man concerned, and sulphuric ether was the substance used. The experiment was quickly repeated by Simpson and his colleagues, and soon by obstetricians in widely different medical centres. The subsequent order of events seems to have been as follows. In France, it was first used on January 27 by Fournier-Deschamps. On February 8, it was employed by Baron Dubois who, on February 23, reported its use to the French Academy of Medicine. In London, it was used on February 13 by Dr. Murphy and, later, by Dr. Prothero Smith. In Germany, Professor Martin of Jena used it on February 24, and in America (the birth-place of ether anæsthesia), it was used on April 7 by Dr. Keep of Boston.

By the introduction of anæsthesia into midwifery it became possible not only to lift at will the pain of labour but—and perhaps this was even more important and significant—to employ, in good time, necessary obstetric operations—operations that hitherto, if used at all, had been used as a desperate effort to save a mother's life when all else had failed, and used with the certain knowledge that the patient would thereby be subjected to almost unendurable suffering.

It is perhaps not now clearly realized how daring the deliberate production of insensibility seemed to the workers of those days. It was at first supposed that the method could be

Section of Orthopædics

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[October 7, 1947]

Pes Planus or Instability of the Longitudinal Arch

PRESIDENT'S ADDRESS

By GEORGE PERKINS, M.C., F.R.C.S.

No subject in orthopædic surgery is more muddling than flatfoot. It is a common experience for an orthopædic surgeon to see in his out-patient department hordes of children sent up from school clinics with a diagnosis of pes planus, children who have perfectly normal feet except that their longitudinal arches are low. One is reluctant to send these children away without treatment, because the mothers have been led to believe that treatment is necessary; and one is often persuaded to order remedial exercises and wedged heels solely in order to relieve the anxiety of the parents. I believe that we are swamping our physiotherapy departments with children who do not require treatment, thereby not only wasting the time of the masseuses, but, more important, laying an additional burden on overworked mothers who have quite enough to do in the day without taking their children up to hospital for treatment.

In my view, the popular term "flatfoot" is misleading, since it does not matter whether the longitudinal arch is high or low. A foot with a high arch is just as likely to cause trouble as a foot with a low arch. The presence or absence of symptoms depends on the degree of stability of the arch. A stable arch, whether high or low, is free of symptoms. A foot with an unstable arch is weak and liable to ache. It is unfortunate that the clinical term "pes planus" is so well established, for it would be better to substitute for it the term "instability of the longitudinal arch".

The condition of flatfoot, or instability of the longitudinal arch, cannot be properly understood without a clear understanding of (1) the respective functions of muscles, ligaments and bones, (2) the structure of the longitudinal arch, and (3) how the stability of the arch is normally preserved.

The functions of muscles, ligaments and bones.—Muscles have two functions: (a) to move a joint, and (b) to place and hold a joint in such a position that stress passes directly through its centre. In this respect, muscles act like the staywires of a wireless mast. The staywires do not themselves support the massive weight of the mast, but by their tension hold the mast vertical and by so doing enable the mast to support itself. And if the tension of the staywires was regulated with sufficient nicety, the mast would still support itself in the upright position even if it were joined in the middle (fig. 1). In the case of a wireless mast, the tension of the staywires has to be regulated by an external agency. Muscles, on the other hand, regulate their own tension. This automatic regulation of muscle tension depends on the sensitivity of the joint ligaments.

The ligaments act as watchdogs, giving warning when a joint is being moved beyond a prescribed range. They cannot themselves resist a force except momentarily, and under sustained tension they stretch. As soon as they are stretched they send an S O S via the afferent nerves to the spinal synapses, calling on the muscles to come into action to resist the stretching force (fig. 2).

expanding sponge tent and the uterine sound—in the form we now know that instrument—Simpson made it possible to explore the cavity of the uterus and thus to make the diagnosis of many abnormalities of that organ a matter of scientific certainty rather than of clinical speculation. He was the first in this country to remove the cervix uteri for carcinoma. In addition to a vast output of very able writings, and his many other activities, Simpson could yet devote time to his favourite study of archæology; and his researches into the history of 160 leper houses in Scotland is a contribution still regarded as the most authoritative of its kind in existence.

Living at a time when public controversy and dispute flourished to an extent that is now hardly credible, Simpson was himself a supreme controversialist. Among the many innovations he proposed, or causes he championed, may be mentioned the use of acupressure (a surgical technique devised by himself whereby hæmorrhage from limb amputations could be controlled without the need for dangerous ligatures), and the building of small, airy, easily demolished wards for the treatment of surgical patients. These two recommendations, it should be noted, were made at a time when Listerian surgery was still many years ahead. He advocated a systematic campaign to stamp out zymotic diseases, and he fiercely denounced the doctrines of homœopathic medicine.

To us in these days it seems incredible that there should have been opposition to anæsthesia. Meigs, Professor of Midwifery in Boston, stated: "Anæsthesia is unnecessary as shown by the birth of past myriads"; elsewhere he described labour pains as "a desirable salutary, and conservative manifestation of life-force". Other authorities declared that anæsthesia was "unnatural"; that it was an "unnecessary interference with the providentially arranged process of healthy labour"; that it would certainly increase the mortality of operations; that it might induce convulsions in the pregnant woman; that it might result in the child delivered of a woman under anæsthesia developing into an idiot; that it was "a decoy of Satan apparently offering itself to bless women, but in the end hardening society and robbing God of the deep, earnest cries which arise in the time of trouble, for help". In short, anæsthesia transgressed the scriptural teaching: *in sorrow thou shalt bring forth children*.

Against this very formidable opposition, Simpson brought all his considerable fighting powers to bear. His pamphlet entitled an "Answer to Religious Objections Advanced Against the Employment of Anæsthetic Agents in Midwifery and Surgery" is an outstanding example of his profundity of study, his powers of logic and his scholarly handling of the questions at issue—in this case, philosophical and theological arguments, and the exact meaning of the Hebrew roots of the words from which the relevant passages of our Bible are translated. For several years opinion regarding anæsthesia in childbirth was sharply divided, then news came to an astonished world that Queen Victoria herself, for the birth of her eighth child, Prince Leopold, had had chloroform administered, and had been well pleased with the result. The battle was won.

Simpson died at the age of 59, a victim of angina pectoris. His last illness was precipitated by the rigours of a double journey to London in the coldest weather of winter, made in response to a citation as an expert witness in a medico-legal case.

This is not the time to enter into a discourse concerning the rival merits of ether and chloroform: it is, however, right to pay fresh tribute to the remarkable man who introduced anæsthesia into midwifery and who, with George Keith and Matthews Duncan, later discovered the anæsthetic properties of chloroform. By their work, and by Simpson's unceasing battle against indifference, prejudice and bigotry, the general adoption of anæsthesia was immensely hastened and the scope of surgical and of obstetric operations immeasurably increased.

[Professor JAMES MILLER also read a paper on James Young Simpson which has been published in the *Journal of Obstetrics and Gynæcology of the British Empire*, 1947, 54, 729.]

modifying, for the anterior pillar comprises two prongs, a medial and a lateral. So that, in fact, the longitudinal arch has three main bearing points, the undersurface of the os calcis, the head of the first metatarsal and the head of the fifth metatarsal (fig. 5). When these three bearing points are all on the ground, the foot is said to be plantargrade. (The arch is further strengthened by a cross support—the cuboid—joining the posterior pillar to the lateral anterior pillar, but this is incidental to the present argument.)

For the longitudinal arch to be stable, two conditions must be fulfilled: (1) the body-weight must pass through the centre of the subtaloid-midtarsal joint and (2) when the body-weight is being transmitted through the centre of the subtaloid-midtarsal joint, the foot must be plantargrade, i.e. all three bearing points must be on the ground.

Causes of instability of the longitudinal arch.—The muscle-ligament reflex balancing mechanism, or as it is sometimes called—the postural activity of muscle—is not present at birth, and is gradually acquired during the first year or two of life. When babies first attempt to walk their feet capsize into plano-valgus. Slowly they acquire the knack of balancing their body-weight through the centre of their longitudinal arch, and the plano-valgus disappears. Like the riding of a bicycle, the knack once

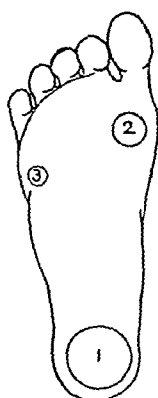


FIG. 5.—The three main bearing points of the foot.



FIG. 6.—Varus forefoot.



FIG. 7.—Varus forefoot masked by valgus heel.

learnt is never forgotten, and for the remainder of life the reflex automatically functions whenever the person stands (granted of course that the muscles, ligaments and reflex arc remain healthy). Sometimes, however, the postural activity of muscle is late in developing, and some children persist in standing with their feet in plano-valgus until the age of 3 or 4. Occasionally for some unexplained reason the postural activity of muscle as regards the subtaloid-midtarsal joint is never acquired, and the longitudinal arch remains unstable throughout life, the foot collapsing into plano-valgus whenever the person stands.

Once the postural activity of muscle has been acquired there can be only one reason for pes planus or instability of the longitudinal arch, viz. that the foot, when at right-angles to the leg, is not plantargrade. In a plantargrade foot the three bearing points—the under surface of the os calcis, the ball of the big toe and the ball of the little toe—are in contact with the ground. Two deviations from this orthodox plantargrade position are common: (a) the posterior pillar may be at fault, and the heel does not touch the ground, i.e. there is an equinus deformity, and (b) the medial anterior pillar may be at fault, and the big toe is off the ground, i.e. there is a varus deformity of the forefoot (fig. 6).

The function of *bone* is in no doubt. Bone is constructed to support weight and to assist stress indefinitely; and its lamellæ are parallel to the lines of force likely to be transmitted. Incidentally, when a stress that is not parallel to the lamellæ falls on a bone the bone often breaks. Most fractures are caused by angulation or torsion; rarely does a bone break under a vertical stress.

In the past there has been great argument about whether the longitudinal arch of the foot is supported by muscles or by ligaments. My contention is, that the longitudinal arch supports itself so long as the muscles balance the joints of the arch in such a way that stress passes through the centre of those joints.

The structure of the longitudinal arch.—The longitudinal arch is a composite bony structure designed to transmit the weight of the body to the ground through a wide basis of support. The talus is the keystone of the arch, the os calcis forms the posterior pillar, and the scaphoid, cuneiforms and metatarsals the anterior pillar (fig. 3). Like any architectural arch the human longitudinal arch is able, owing to

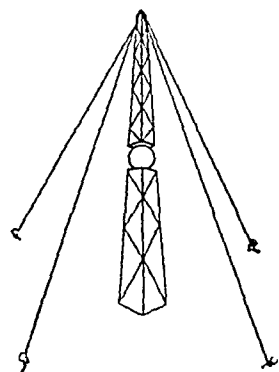


FIG. 1.—Hinged wireless mast, held erect by staywires.

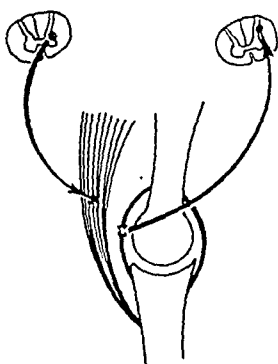


FIG. 2.—The ligament-muscle reflex mechanism.

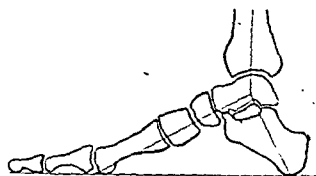


FIG. 3.—The longitudinal arch, in its stable condition.

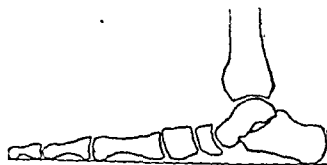


FIG. 4.—The longitudinal arch, when unstable.

its configuration, to transmit weight without collapsing. When a normal person stands, the weight of his body is transmitted to the ground via the bones of the longitudinal arch; neither ligaments nor muscles transmit any of the stress. One has only to palpate the leg of a standing person to discover that the leg muscles are not in vigorous action. Yet, although the muscles and ligaments do not themselves support any weight, they are essential factors in preserving the stability of the longitudinal arch because the longitudinal arch is a jointed structure. The main joint is a composite affair comprising the subtaloid and the midtarsal articulations. This composite joint capsizes unless weight is transmitted directly through its centre (fig. 4).

When weight is transmitted directly through the centre of the subtaloid-midtarsal joint, all the stress passes through the bones. On the other hand, when weight does not pass directly through the centre of the joint, the ligaments are subjected to tension. The ligaments, on being stretched, reflexly call into action the muscles. Whereupon the muscles alter the position of the subtaloid-midtarsal joint until stress again passes through the centre of the joint. The muscles and ligaments thus form a balancing mechanism which ensures that the weight is transmitted to the ground through the bones without any strain being thrown on the joints of the longitudinal arch.

How the stability of the arch is normally preserved.—I have said that the longitudinal arch consists of a keystone and anterior and posterior pillars. This statement needs

modifying, for the anterior pillar comprises two prongs, a medial and a lateral. So that, in fact, the longitudinal arch has three main bearing points, the undersurface of the os calcis, the head of the first metatarsal and the head of the fifth metatarsal (fig. 5). When these three bearing points are all on the ground, the foot is said to be plantargrade. (The arch is further strengthened by a cross support—the cuboid—joining the posterior pillar to the lateral anterior pillar, but this is incidental to the present argument.)

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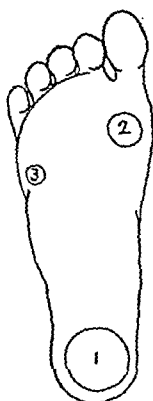


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An equinus, when present, is compensated for, when the person stands, by dorsiflexion at the subtaloid-mid tarsal joint, but dorsiflexion at this composite joint is accompanied by eversion. Although the foot becomes plantargrade by this means, it does so at the expense of a malalignment of the body-weight, which no longer passes through the centre of the subtaloid-mid tarsal joint.

Varus deformity of the forefoot is compensated for by eversion at the subtaloid-mid tarsal joint (fig. 7) and again the foot is rendered plantargrade at the expense of malalignment of the body-weight.

Equinus has long been recognized as a cause of flatfoot but until recently varus deformity of the forefoot has been overlooked as a causative factor. Both deformities are common. Their origins are obscure. They might result either from a fault in the growth of the tarsal bones, or more likely from the growth of the muscles failing to keep pace with the growth of the skeleton.

In the case of an equinus the calf muscles do not lengthen as quickly as the tibia, and in the case of a varus forefoot the increase in length of the tibialis anticus does not keep pace with the growth of the tibia and tarsus.

Thus, the three main causes of pes planus or instability of the longitudinal arch are: (1) Faulty postural activity of muscle, (2) an equinus deformity of the whole foot, and (3) a varus deformity of the forefoot.

There is, in addition, a congenital type of flatfoot, the skiagram of which shows the talus to be in equinus and the forefoot in marked dorsiflexion. This congenital deformity is rare, and is unlikely to be confused with ordinary pes planus because the shape of the foot is not natural; the sole is boat-shaped. There is also another condition, named spasmodic pes planus, but this is probably an arthritis of the subtaloid joint and not a mechanical instability of the longitudinal arch. The visible muscle spasm and the complete immobility of the subtaloid joint render the diagnosis unmistakable.

SYMPTOMS

The patient, if an adult, complains that his arches have dropped. He has made his own diagnosis and usually brings with him a pair of Scholl's supports which have failed to give him relief. Pain is felt in the sole and along the medial border of the foot, and the feet get hot and sweaty after standing. Stiffness and lameness are complained of, bad first thing in the morning, better during the day and worse again in the evening. There is often aching up the shins, due to over-use of muscles that are trying to protect the sensitive ligaments. A child usually has no symptoms. Either the parent seeks advice on account of the deformity of the child's feet, or else the child is sent up by a school doctor because the feet appear flat.

CLINICAL TYPES

From the point of view of treatment four types of pes planus or instability of the longitudinal arch deserve recognition: (1) Mobile pes planus, due to faulty postural activity of muscle. (2) Mobile pes planus due to an equinus deformity of the whole foot. (3) Mobile pes planus, due to a varus deformity of the forefoot. (4) Rigid pes planus, in which, owing to the faulty transmission of weight through the subtaloid-mid tarsal joint over a long period, the joint wears out prematurely, degenerative changes set in, and the range of movement dwindles on account of an inelastic sclerosis of the joint capsule.

CLINICAL EXAMINATION

Whenever a person has painful feet he imagines he is suffering from pes planus. Frequently he is not. And the first thing to find out is whether there is a pes planus, i.e. whether there is instability of the longitudinal arch, and then to decide on its type.

The examiner investigates four points: (1) When the patient stands, is there instability of the longitudinal arch? (2) If so, does the arch become stable when he tiptoes? (3) When the patient sits, is the subtaloid-midtarsal joint mobile? (4) If so, is the foot plantargrade when the arch is placed in the stable position?

Is the longitudinal arch stable on standing?—The longitudinal arch is stable when the body-weight passes through the centre of the subtaloid-midtarsal joint. Accordingly, the patient is asked to stand with the feet and knees bare, and the line of weight is inspected. A line drawn from the centre of the knee through the middle of the ankle and projected forwards should pass through the second toe (fig. 8). If it does, well and good. There is no instability of the arch. But the converse is not true; the foot may be externally rotated on the leg, that is, the line of the body-weight may pass medial to the medial border of the foot, and yet the arch may be stable. External rotation of the foot can result from the capsizing of the subtaloid-midtarsal joint (fig. 9), and it can result from anatomical anomaly, which may be

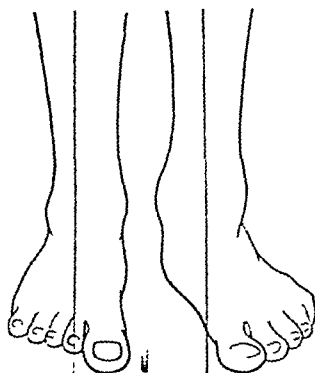


FIG. 8.

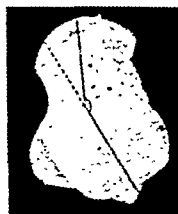


FIG. 10A.

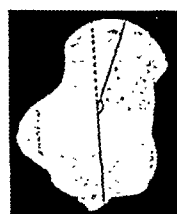


FIG. 10B.

FIG. 8.—Normal line of body-weight.

FIG. 9.—External rotation of the foot due to instability of the longitudinal arch. Line of body-weight falls medial to medial border of foot.

FIG. 10.—(A) Longitudinal axis of astragalus pointing outwards instead of directly forwards. (B) Showing normal angle between the body and the neck of the astragalus.

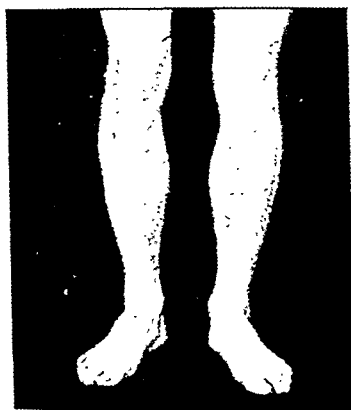


FIG. 11.



FIG. 12.

FIG. 11.—External rotation of foot on leg: yet, the longitudinal arch is stable.

FIG. 12.—Normal alignment of body-weight on the right. Eversion of the heel (and therefore instability of the longitudinal arch) on the left.

one of two kinds. In the first, the long axis of the body of the talus points slightly outwards instead of directly forwards (fig. 10). In the second, although the body of the talus is directed straight forwards, the angle the body makes with the neck is abnormal. The anatomists tell us that the neck makes an angle of 140 degrees with the body, so that the anterior surface of the talus which articulates with the scaphoid

faces slightly inwards. In many tali, the angle is nearer 180 degrees than 140 degrees and the anterior articular surface points forwards. Which of these two anomalies is the more common I do not know, but certain it is that in many people, who make no complaint about their feet, the foot is externally rotated on the leg (fig. 11). This external rotation is, in my experience, particularly common among Jews.

What, therefore, we have to decide, in the presence of an externally rotated foot, is whether the external rotation is an anatomical anomaly or whether it is due to a capsizing of the subtaloid-midtarsal joint. To make the decision, one views the standing patient from behind, and draws an imaginary line down the middle of the leg. In the normal person this line deviates slightly outwards at the ankle, but if the os calcis is not directly under the talus, that is, if there is eversion at the subtaloid joint, the line angulates grossly outwards (fig. 12).

It needs to be emphasized that during this examination no attention is paid to the height of the longitudinal arch; all we are concerned with is its stability.

Can the stability of the longitudinal arch be restored?—The patient is asked to stand on tiptoe, and again the line of the body-weight is inspected. If it still passes medial to the second toe, the pes planus is of the rigid type. In the other three types the stability of the longitudinal arch is restored, and the line of the body-weight passes through the second toe.

In the type of pes planus due to faulty postural activity of muscle, the voluntary contraction of the plantar flexors of the foot balances the subtaloid-midtarsal joint so that weight passes through its centre. Stability to the longitudinal arch is likewise automatically restored if the instability is due to an equinus. When the pes planus is caused by a varus deformity of the forefoot, stability is also restored by the vigorous voluntary contractions of the leg muscles, but the patient takes his weight almost entirely through the lateral anterior pillar of the longitudinal arch, and the big toe comes off the ground. With all the weight passing through a single bearing point, the patient is not very steady, and he cannot stand on tiptoe on one foot alone.

Is the subtaloid joint mobile?—The patient is now examined recumbent, with the feet passive. The heel is held by the surgeon in a central position (neither varus nor valgus) and the forefoot placed so that the line of the body-weight passes through the second toe. If this cannot be done, the subtaloid-midtarsal joint has lost its normal mobility, and the pes planus is of the rigid type. There is fixed deformity at the subtaloid-midtarsal joint, which is everted, abducted and dorsiflexed. The eversion is difficult to see because it is masked by a compensatory varus of the forefoot, and the three bearing points are on the same plane. The abduction is made obvious by the uncovering of the neck of the astragalus. On the medial border of the normal foot there is a hollow between the two bony lumps that are formed by the internal malleolus and the tubercle of the navicular respectively. When the foot is abducted the hollow is replaced by a third lump produced by the uncovered neck of the astragalus.

Finally, is the foot plantargrade?—In the three mobile types of pes planus, the foot can be placed so that the line of the body-weight passes through the second toe. The surgeon correctly aligns the foot and then directs his attention to the three bearing points. In pes planus due to faulty postural activity of muscle, the foot is plantargrade, i.e. all three bearing points are in a plane that is at right-angles to the leg and also at right angles to the couch. In the other two types of pes planus the foot is not plantargrade, either an equinus deformity or a varus deformity of the forefoot is disclosed (figs. 13A and 13B).

Clinical signs of the four different types of pes planus.—These may be summarized as follows:

(1) *Pes planus due to faulty postural activity of muscle:* There is malalignment of the body-weight when the patient stands, but this disappears when he tiptoes. In

the recumbent position the foot is mobile, and when the foot is correctly aligned, it is plantargrade.

(2) *Pes planus due to an equinus*: There is malalignment of the body-weight which disappears on tiptoeing. The foot is mobile, but the foot when correctly aligned is in equinus.

(3) *Pes planus due to a varus deformity of the forefoot*: The malalignment of the body-weight disappears on tiptoeing, but the patient finds it hard to balance because he is taking all his weight on a small bearing area. The foot is mobile, but when it is correctly aligned the forefoot is in varus.

(4) *Rigid pes planus*: The malalignment does not disappear when the patient tiptoes. The foot is rigid and cannot be correctly aligned when the patient is recumbent. There is fixed eversion, abduction and dorsiflexion at the subtaloid-midtarsal joint. The foot is, however, plantargrade, for the eversion is compensated for by a varus of the forefoot. There is an accessory lump on the medial border of the foot formed by the uncovering of the neck of the talus.

TREATMENT

For mobile pes planus due to faulty postural activity of muscle.—It is natural for an infant to stand at first with its feet in plano-valgus. Pes planus at this age needs no treatment, for the child gradually acquires the knack of balancing his body-weight through the centre of his subtaloid-midtarsal joint. If postural activity is late in developing and pes planus persists after the age of 2, it is the almost universal practice to wedge the heels of the shoe. But this is a fatuous procedure because a baby's shoe never grips the heel of the foot, which remains in valgus inside the shoe. The deformity is masked not corrected. Wedging of a shoe is justifiable as a placebo when the surgeon feels confident that treatment is not necessary. If treatment is really essential the child must wear boots, which if effectively wedged—and often more than the customary three-sixteenths of an inch is needed—will hold the heel of the foot in varus. Wedging the sole of the boot is unnecessary and often harmful, and moreover makes the sole rigid and renders a toe-and-heel gait difficult. I see no point in the forward prolongation of the heel. It is said that a few children never learn to balance their weight correctly through their feet, with the result that the subtaloid-midtarsal joint becomes hypermobile. Pes planus with hypermobility of this balancing joint is not infrequently seen, but in my experience there is almost always an associated and causative foot deformity, either an equinus or a varus forefoot.

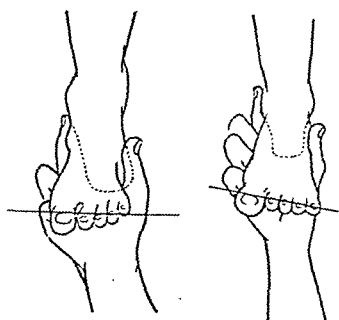


FIG. 13A.

FIG. 13B.

FIG. 13A.—Varus forefoot invisible on account of valgus heel. B.—With heel placed in the central position, varus deformity of the forefoot is disclosed.

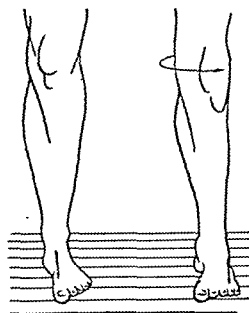


FIG. 14.—Shifting of the line of the body-weight laterally by external rotation of the leg.

It has always been customary to treat mobile flatfoot with exercises. A simple exercise is prescribed which the child can carry out many times during the day until

faces slightly inwards. In many tali, the angle is nearer 180 degrees than 140 degrees and the anterior articular surface points forwards. Which of these two anomalies is the more common I do not know, but certain it is that in many people, who make no complaint about their feet, the foot is externally rotated on the leg (fig. 11). This external rotation is, in my experience, particularly common among Jews.

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Can the stability of the longitudinal arch be restored?—The patient is asked to stand on tiptoe, and again the line of the body-weight is inspected. If it still passes medial to the second toe, the pes planus is of the rigid type. In the other three types the stability of the longitudinal arch is restored, and the line of the body-weight passes through the second toe.

In the type of pes planus due to faulty postural activity of muscle, the voluntary contraction of the plantar flexors of the foot balances the subtaloid-midtarsal joint so that weight passes through its centre. Stability to the longitudinal arch is likewise automatically restored if the instability is due to an equinus. When the pes planus is caused by a varus deformity of the forefoot, stability is also restored by the vigorous voluntary contractions of the leg muscles, but the patient takes his weight almost entirely through the lateral anterior pillar of the longitudinal arch, and the big toe comes off the ground. With all the weight passing through a single bearing point, the patient is not very steady, and he cannot stand on tiptoe on one foot alone.

Is the subtaloid joint mobile?—The patient is now examined recumbent, with the feet passive. The heel is held by the surgeon in a central position (neither varus nor valgus) and the forefoot placed so that the line of the body-weight passes through the second toe. If this cannot be done, the subtaloid-midtarsal joint has lost its normal mobility, and the pes planus is of the rigid type. There is fixed deformity at the subtaloid-midtarsal joint, which is everted, abducted and dorsiflexed. The eversion is difficult to see because it is masked by a compensatory varus of the forefoot, and the three bearing points are on the same plane. The abduction is made obvious by the uncovering of the neck of the astragalus. On the medial border of the normal foot there is a hollow between the two bony lumps that are formed by the internal malleolus and the tubercle of the navicular respectively. When the foot is abducted the hollow is replaced by a third lump produced by the uncovered neck of the astragalus.

Finally, is the foot plantargrade?—In the three mobile types of pes planus, the foot can be placed so that the line of the body-weight passes through the second toe. The surgeon correctly aligns the foot and then directs his attention to the three bearing points. In pes planus due to faulty postural activity of muscle, the foot is plantargrade, i.e. all three bearing points are in a plane that is at right-angles to the leg and also at right angles to the couch. In the other two types of pes planus the foot is not plantargrade, either an equinus deformity or a varus deformity of the forefoot is disclosed (figs. 13A and 13B).

Clinical signs of the four different types of pes planus.—These may be summarized as follows:

(1) *Pes planus due to faulty postural activity of muscle:* There is malalignment of the body-weight when the patient stands, but this disappears when he tiptoes. In

the recumbent position the foot is mobile, and when the foot is correctly aligned, it is plantargrade.

(2) *Pes planus due to an equinus*: There is malalignment of the body-weight which disappears on tiptoeing. The foot is mobile, but the foot when correctly aligned is in equinus.

(3) *Pes planus due to a varus deformity of the forefoot*: The malalignment of the body-weight disappears on tiptoeing, but the patient finds it hard to balance because he is taking all his weight on a small bearing area. The foot is mobile, but when it is correctly aligned the forefoot is in varus.

(4) *Rigid pes planus*: The malalignment does not disappear when the patient tiptoes. The foot is rigid and cannot be correctly aligned when the patient is recumbent. There is fixed eversion, abduction and dorsiflexion at the subtaloid-midtarsal joint. The foot is, however, plantargrade, for the eversion is compensated for by a varus of the forefoot. There is an accessory lump on the medial border of the foot formed by the uncovering of the neck of the talus.

TREATMENT

For mobile pes planus due to faulty postural activity of muscle.—It is natural for an infant to stand at first with its feet in plano-valgus. *Pes planus* at this age needs no treatment, for the child gradually acquires the knack of balancing his body-weight through the centre of his subtaloid-midtarsal joint. If postural activity is late in developing and *pes planus* persists after the age of 2, it is the almost universal practice to wedge the heels of the shoe. But this is a fatuous procedure because a baby's shoe never grips the heel of the foot, which remains in valgus inside the shoe. The deformity is masked not corrected. Wedging of a shoe is justifiable as a placebo when the surgeon feels confident that treatment is not necessary. If treatment is really essential the child must wear boots, which if effectively wedged—and often more than the customary three-sixteenths of an inch is needed—will hold the heel of the foot in varus. Wedging the sole of the boot is unnecessary and often harmful, and moreover makes the sole rigid and renders a toe-and-heel gait difficult. I see no point in the forward prolongation of the heel. It is said that a few children never learn to balance their weight correctly through their feet, with the result that the subtaloid-midtarsal joint becomes hypermobile. *Pes planus* with hypermobility of this balancing joint is not infrequently seen, but in my experience there is almost always an associated and causative foot deformity, either an equinus or a varus forefoot.

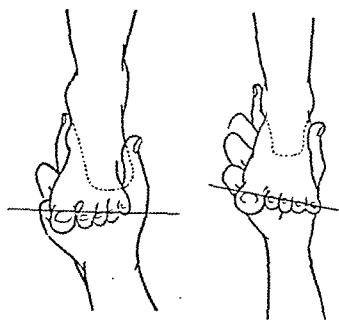


FIG. 13A.

FIG. 13B.

FIG. 13A.—Varus forefoot invisible on account of valgus heel. B.—With heel placed in the central position, varus deformity of the forefoot is disclosed.

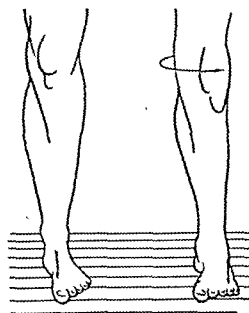


FIG. 14.—Shifting of the line of the body-weight laterally by external rotation of the leg.

It has always been customary to treat mobile flatfoot with exercises. A simple exercise is prescribed which the child can carry out many times during the day until

it becomes automatic; the idea being to encourage the acquisition of an involuntary postural reflex by a conscious voluntary muscle effort. Whether postural activity can be acquired in this way is doubtful. In any case, the usual form of exercise—standing on the outer border of the foot by contracting the *tibialis anticus*—is objectionable because it conduces to a varus forefoot. A better exercise, although more difficult to teach a young child, is to make the patient rotate out the legs while keeping the feet flat on the ground (fig. 14). External rotation of the leg on the foot is equivalent to internal rotation of the foot on the leg, which is what we want to encourage. Making the child stand and walk pigeon-toed is another good exercise.

For pes planus due to an equinus.—It would seem obvious to treat this type of pes planus by exercises designed to stretch the calf muscles. Unfortunately, the stretching force cannot be confined to the ankle-joint and acts also on the subtaloid-midtarsal joint, which it thrusts into eversion, abduction and dorsiflexion. The calf muscles may eventually be lengthened but at the same time the subtaloid-midtarsal joint has been made more wobbly and more difficult for the postural muscle reflex to control. It is better, therefore, in boys, to overcome the equinus by a subcutaneous lengthening of the tendo Achillis; and while the tendon is repairing, to immobilize the foot for six weeks in plaster, with the three bearing points in the same plane, the body-weight correctly aligned, and the foot dorsiflexed to 10 degrees beyond the right-angle. It is by no means easy to apply the plaster with the foot in

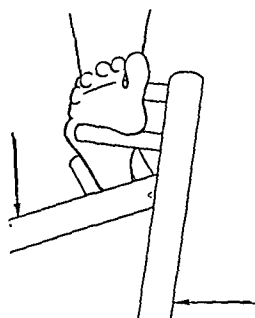


FIG. 15.—Two Thomas's wrenches used to correct varus forefoot.

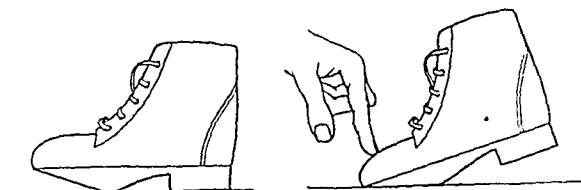


FIG. 16.—Rockered plaster over-boot.

the correct position. Elongation of the tendo Achillis, while not noticeably weakening the calf muscles, does alter the shape of the calf, and the operation is on this account contra-indicated in girls. In them, the equinus should be compensated for by raising the heel of the shoe. This simply anticipates the time when they will naturally wear a high-heel shoe. The rationale of the treatment has to be explained to school mistresses who are apt to object to their pupils not wearing the regulation low-heel shoes of childhood.

For pes planus due to varus forefoot.—We are here dealing with an architectural defect of the longitudinal arch. The arch, when the foot is correctly aligned so that the body-weight passes through the centre of the subtaloid-midtarsal joint, has only two of its three bearing points on the ground; and the problem is to get all three on the ground. This can be done by a forcible manipulation under anaesthesia, at which the medial border of the front part of the foot is thrust downwards. It is interesting to note that some bone-setters empirically use this *manœuvre* in treating flat feet. In resistant cases the aid of two Thomas's wrenches is invoked; one of which grips the os calcis horizontally to hold the heel inverted, while the other grips the forefoot vertically and rotates it into valgus (fig. 15). As a rule it is necessary to immobilize the longitudinal arch in the corrected position for some weeks. Accordingly after the manipulation the foot is put into plaster, with the heel inverted as much as possible, the forefoot everted as much as possible and the whole foot at right-angles

to the leg. The plaster is difficult to apply correctly, and it is helpful to put it on in two stages. The heel is first strapped into full inversion and plastered in this position, and then when this has set the remainder of the foot is included in plaster. A rockered overshoe is fitted over the plaster and the patient is taught to walk with a natural gait (fig. 16). By this means the muscles are prevented from wasting and the joints remain mobile, so that when the plaster is removed at the end of six weeks little rehabilitation is required.

For rigid pes planus.—Here, as well as a structural abnormality of the longitudinal arch there is a fixed deformity at the subtaloid-mid tarsal joint. Both are capable of being remedied by forcible manipulation under anæsthesia; the subtaloid joint can be mobilized, so that the foot is correctly aligned and the body-weight passes through the centre of the subtaloid-mid tarsal joint, and the foot can be made plantargrade by forcible eversion of the forefoot. But often when this has been done movement at the subtaloid-mid tarsal joint is limited and painful, and walking is uncomfortable and remains so until movement is abolished by ankylosing the subtaloid joint. If, however, the subtaloid joint is to be arthrodesed there is no need to correct the alignment of the foot, and even were this necessary it could be accomplished at the same time as the subtaloid-mid tarsal joint was arthrodesed. Therefore, for a rigid pes planus that is causing pain, arthrodesis of the subtaloid-mid tarsal joint is advisable. When the fusion is solid and the foot is released from plaster, the dorsiflexion stress that necessarily accompanies the act of ordinary walking is abolished by rockering the sole of the shoe, as is done in a wooden-soled utility shoe.

Before resorting to an arthrodesis, however, it is worth while seeing whether one can make the patient comfortable by supporting the medial border of his foot. If the upper of the shoe is made rigid, the body-weight can often be transmitted to the ground through the medial border of the foot. Herein lies the value of the rigid foot support. The support is usually made of metal, as in the well-known Scholl's support; but as likely as not this will be superseded in the future by some plastic material which can be moulded to the contour of the medial and under surfaces of the foot. As yet no plastic material of sufficient strength is available.

Mr. W. Sayle-Creer agreed with Mr. Perkins in his advocacy, perhaps unintentional, of more frequent surgical intervention. There were two schools of thought about the maintenance of the long arch—was it by muscles or by ligaments? He felt the application of Sherrington's work on reflex and postural action to the foot had been a disservice to many patients. The experiments of D. J. Morton and Norman Lake suggested the supporting action of the ligaments was of importance. Mr. Perkins had accepted the half-way view of MacConaill that the ligaments were watchdogs and initiated reflex call to muscles if stretched or liable to stretch. But Mr. Perkins had previously demonstrated beautiful results of dividing ligaments to cure the reverse type of condition, talipes equino-cavo-varus. If the ligaments were not important in themselves, where was the need to divide them?

Mr. Perkins stated that the arch supports itself. But this was too ambiguous if unqualified. The stones of an architectural arch were held together by mortar and gravity, and something must hold together the bones of the foot. It might be suction (vacuum) of the joints; more likely it was the ligaments.

He complimented the speaker on his criticism of the term, flat foot. "Instability" was a good description; however, he preferred the American term, *Pronation*, because that described the complicated deformity best. It was stimulating to hear of the other factors, e.g. tightness of tendo Achillis, overaction of tibialis anticus. These were usually overlooked by British writers. He agreed with Mr. Perkins on the ineffectiveness of physiotherapy as usually given. There was no doubt that a surgical operation was much better than surgical footwear in many cases, but he deprecated any rush to operate. However, operations such as those of Lambrinudi were already being done and he felt sure that in future more and more would be performed.

Mr. E. T. Bailey said that in adolescents and adults the symptoms of foot strain ascribed to so-called "flatfoot" were due frequently to imbalance of the foot in a varus position, secondary to a varus deformity of the forefoot. This varus deformity prevented adequate depression of the head of the first metatarsal to the ground by foot pronation, using the term in a descriptive rather than in a strict anatomical sense. Deficient foot pronation meant that the head of the first metatarsal could only be brought to the ground by a valgus tilting of the heel at the sub-astragaloid joint with a resulting valgus deviation of the foot as a whole, giving a typical picture of "flatfoot".

The logical treatment of valgus foot strain lay in foot re-education. For this purpose the usually accepted exercises were inadequate and the assistance of an appropriate exercising machine, such as the Harrens' foot corrector designed for this purpose, could be of material help and had, in practice, proved capable of restoring some 20 to 30 degrees of deficient pronation over a period of some three weeks of treatment.

Sir Thomas Fairbank said he was particularly glad to hear the President refer to fixed inversion of the forefoot on the hindfoot as a factor in many cases. For many years past he had waited in vain for this important point to be referred to in a textbook. This inversion was often difficult to correct. He also welcomed the President's advice that the sole of the boot should not be wedged, but only the heel: he well remembered having an argument with Sir Robert Jones on this point. In young children of over 2 years, he had found the use of removable leather-covered cork valgus insoles in the boots of the greatest value. Though theoretically pressure on the muscles in the sole was inadvisable, he had found these "supports" cure many cases before they were old enough to co-operate in the treatment, a result achieved in only a few cases by simple heel-wedging alone. He preferred postural drill to exercises for the older children. Teaching the child how to stand and walk properly, and persisting in this till the correct posture of the feet had become habitual, he regarded as the only physical treatment of value: ordinary exercises alone he had found of no value.

Mr. J. A. Cholmeley remarked that it was very rare for any shoes or boots to fit a person, particularly a child, closely, as a glove, and in consequence he did not believe that wedging a shoe would have any marked influence on the foot itself but rather that the foot takes up its natural position in the shoe and fitting of an appropriate wedge merely ensures that the shoe or boot shall wear level.

He also stated that at the present time children's footwear is extremely bad and that the soles are generally so stiff that it is necessary to apply considerable force in order to bend them and make them pliable at all.

Mr. J. S. Batchelor said that flatfoot was an unsatisfactory term, for the majority of patients alleged to suffer from this condition showed a postural valgus deformity of the foot without any actual decrease in the height of the long arch. True flatfoot was relatively uncommon and was essentially a congenital deformity.

A valgus foot posture was often associated with an equinus deformity, often rather loosely described as a contracture of the tendo Achillis, and it was unfortunate that the routine remedial exercises usually prescribed strengthen rather than relax the calf muscles. In acute spasmodic valgus, equinus deformity was almost invariably present, and unless this was corrected during the period of immobilization in plaster by placing the foot in a dorsiflexed position, relapse was likely to occur after the plaster was removed.

Mr. V. C. Snell said that he would like to support the suggestion of Mr. Batchelor, that the first group described by Mr. Perkins should not be referred to as "flatfoot", since the deformity occurred at the subastragaloid joint, and there was no actual flattening of the foot itself.

He then referred to the opinions of Mr. McCrae Aitken with regard to this deformity.

When considering postural deformities it must be remembered that the foot is, to some extent, fixed on the ground. The leg moves on the foot, the thigh on the leg, and so on. In consequence, the muscles concerned in maintaining this posture may be regarded as having their origin below and their attachment above.

The astragalus may form part of the leg or part of the foot. In the latter case the tibia hinges on the astragalus and moves backwards or forwards. In the former case the astragalus is locked in the mortice between the tibia and fibula, and together they rotate inwards or outwards on the os calcis.

Normally this internal rotation which would be produced by the body-weight is prevented by the tibialis posticus as it passes round the inner side of the astragalus and behind the medial malleolus. It will occur if the tone of the tibialis posticus is insufficient to oppose the body-weight, and the deformity which we are discussing is thus produced. It is essentially a valgus or internal rotation deformity, and the long arch of the foot is hidden, though the relative position of the bones composing it is little affected.

This same internal rotation underlies hallux valgus, genu valgum, and to some extent postural scoliosis. Each is due to insufficiency of the postural muscles compared with the load they sustain. None of these conditions should really be considered apart from the others.

The tendency to this deformity will be increased by overweight or by insufficiency of tone of the postural muscles which is often due to some illness. If the tibialis posticus remains insufficient the patient may attempt to relieve the strain by using the tibialis anticus and the long extensor of the big toe, neither of which is designed to maintain posture. This may underlie the deformity also described by Mr. Perkins where there is a varus deformity of the forefoot.

As regards treatment, if the valgus position is corrected when the patient stands on tiptoe (i.e. on active contraction of the tibialis posticus) it is enough to relieve the strain on this muscle by heel wedges until it has had time to get stronger. Heel wedges are efficient if care is taken that the shoes fit adequately around the hindfoot.

Clinical Section

President—G. E. VILVANDRÉ

[October 10, 1947]

Two Cases of Coarctation of Aorta.—A. DICKSON WRIGHT, M.S.

I.—Miss A., aged 33; land worker.

Family history.—Not significant. As a child she suffered from bilious attacks. Eight years ago intermittent encephalopathic symptoms appeared and were often quite disabling. The headaches were a general pain over the head associated with vomiting and were relieved by bandaging the head tightly. The vertigo was sometimes very severe and even caused fainting. The eyes were watery and the vision blurred. The legs were noticed to be cold in their lower halves and walking caused claudication. Pounding of the heart was a distressing symptom and interfered with sleep, and anginal pains radiating into both arms and breathlessness on exertion were diagnosed as asthma.

On examination.—Loud systolic murmur could be heard over the whole area of heart but was loudest posteriorly. Collateral vessels seen pulsating on chest and in scapular region when patient bent forward (Susman's sign) and the murmur was conducted along these vessels. The radial pulses were equal and normal but the femoral pulses could not be felt. Blood-pressure was elevated but labile, at times it exceeded 300 but after rest in bed for seven days it fell to 140. With sodium amytal test it fell significantly. X-ray showed absence of aortic bulge and notching of ribs (4, 5, 6) and the descending aorta below coarctation dilated. Blood urea 33 mg.

Although referred for sympathectomy, resection of the stenosis was thought preferable and from this she made a good recovery. The blood-pressure is now normal; and pulses at the ankle are easily felt. There was still a slight murmur in the region, and this was expected as the aorta above the coarctation was only about half the diameter of the descending aorta. This murmur has now disappeared.

II.—Miss C., aged 36; secretary.

Family history.—Her mother, who died suddenly at 70, had all her life, visible pulsation in the neck such as the patient displayed. Patient's symptoms for past six years consisted of periodic attacks of blurring of vision, pounding of heart and visible pulsation in the neck. The blood-pressure labile, sometimes as low as 160 and very often as high as 370 mm.Hg. The eye grounds showed silver wire arteries and pallor of the retina. X-ray of the thorax showed the usual picture of no aortic knuckle and indentations of the lower rib margins. Blood urea 44 mg. Femoral pulses could only be felt with difficulty and were delayed as compared with radial pulse. Blood-pressure in legs were about one-half of arm pressures. Loud systolic murmur. Susman's sign was well shown in addition.

The patient had come in to hospital for ligature of varicose veins but consented to the major procedure.

The operation was straightforward except that the ductus was quite patent and as much blood seemed to traverse this as the aortic stenosis. The ductus was ligatured and divided and the aortic stricture excised after mobilization of the aorta which was effected by ligature and division of the enlarged intercostal arteries. Recovery was uneventful and after ten days the varicose veins were ligatured. The patient was discharged on the fourteenth day with normal ankle pulses and blood-pressure. The neck pulsation persists but is not so obvious, the visual troubles have disappeared and the palpitation no longer disturbs her rest.

JAN.—CLIN. 1.

The logical treatment of valgus foot strain lay in foot re-education. For this purpose the usually accepted exercises were inadequate and the assistance of an appropriate exercising machine, such as the Harrens' foot corrector designed for this purpose, could be of material help and had, in practice, proved capable of restoring some 20 to 30 degrees of deficient pronation over a period of some three weeks of treatment.

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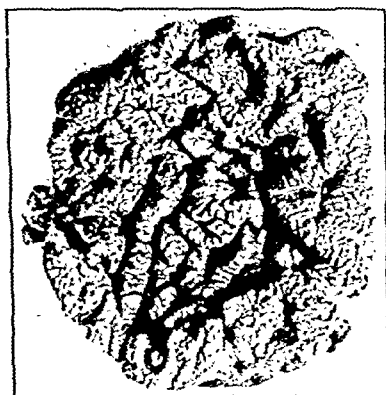


FIG. 1.

Treatment by transfusions, fersolate and multivite: with routine treatment of amœbiasis.

Operation (Mr. Forrester Wood) on August 11, 1947: Elective total gastrectomy by abdomino-thoracic approach. The stomach was much enlarged and had the texture of an enormous varicocele. The pre-operative diagnosis had been probable diffuse neoplasm, and removal was performed as planned.

Comment.—This is a typical example of giant hypertrophic gastritis (Maimon, *et al.*) and the photograph (fig. 1) shows the characteristic appearance of "cerebral convolutions" described in the early reports of the condition by Menetrier. No characteristic symptoms attach to the condition, and its relation to the commoner cases of localized giant rugæ is uncertain. The patient's present condition is excellent.

REFERENCE

MAIMON, BARTLETT, HUMPHREY AND PALMER (1947) Giant Hypertrophic Gastritis, *Gastro-enterology*, 8, 397.

Sclerodactylia with Œsophageal Lesion.—W. A. BOURNE, M.D. (*see Proc. R. Soc. Med.*, 1947, 40, 463. Case I).

The patient developed increasing dysphagia apparently due to pharyngeal inco-ordination, and died suddenly.

Post-mortem examination.—Externally, fairly marked kyphosis with finger nails deformed and brittle and the skin over the thenar eminences and forearms thickened and desquamating. Internally, *tongue smooth*: *œsophagus*, the upper end appeared normal but at the lower end its gross appearance was peculiar, with gradually increasing thickness and opacity of the epithelium, which became white and coarse in texture (leukoplakia) down to the œsophago-gastric junction. This was clearly defined by a sharp transition from the white œsophageal mucosa to the normal-coloured gastric mucosa. A small scar in the lower œsophagus appeared to indicate the site of a healed ulcer. There was a fairly marked hernia of the stomach through the œsophageal hiatus. *Lungs*, basal œdema and early bronchopneumonia; fine bilateral pleural adhesions. *Heart*, very small, the myocardium brown and atrophic, with pericardial thickening and adhesions between visceral and parietal layers. *Small and large intestine*, a curious appearance—generalized thinning and dilatation of the walls of the gut so that it appeared paper thin and of an opaque yellowish colour. There was dilatation of the lacteals, which were visible running through the mesentery. The sigmoid colon showed a few diverticula.

Microscopically, the œsophagus shows little abnormality. The covering epithelium tends to be hyperplastic but has much variation in the depth of the squamous layer. There is patchy round-celled perivascular infiltration in the corium. *Pericardium*: similar perivascular infiltration with hyperplasia of the muscle-cells of the medium-sized vessels. *Myocardium*: fibrous tissue increase and patchy muscle-cell destruction with replacement in some areas by a fine collagenous matrix. *Intestine and mesentery*: no definite histological abnormality.

Comment.—In addition to gross changes in the hands there is evidence of a diffuse change affecting the intestinal tract and pericardium and probably heart muscle and pleura. A clinical diagnosis of small intestine involvement had been made and macroscopical evidence of lacteal obstruction supported this, though clear histological demonstration of excess of collagenous tissue in the mesentery seems difficult in the absence of normal standards. The case is important as an example of the association of sclerodactylia with visceral lesions, which are less common, less demonstrable, or have less time to develop, in diffuse scleroderma with its probably more rapid course.

Myelosclerosis.—D. G. FERRIMAN, D.M.

F. B., a boy aged 13 years, was admitted to the North Middlesex County Hospital on 17.4.47 complaining of pallor and weakness for one week following coryza two weeks beforehand.

Cooley's Anæmia.—J. RUBIE, M.B., M.R.C.P. (for Dr. A. JACOBS).



FIG. 1.

Cooley's anæmia—typical facies.

E. P., aged 9 months. Admitted at 3 months with cough and persistent chronic rhinitis.

Points of interest are.—Parents are Cypriots. The child has anæmia. Blood-count after two months' iron was R.B.C. 5,220,000; Hb 60%; C.I. 0.58; W.B.C. 17,000 (polys. 59%, eosinos. 1%, lymphos. 29%, large monos. 11%); reticulocytes less than 1%; i.e. low Hb and leucocytosis. Target cells in film. R.B.C. show marked decreased fragility—hemolysis commenced 0.32% NaCl, complete at 0.12% NaCl. Mongoloid facies (see figure), muddy complexion. Spleen just palpable. Marrow shows normoblastic hyperplasia. W.R. negative. X-ray of skull shows early changes in frontal bone—the characteristic spicule formation—and there is probably some rarefaction of heads of femora. The father and one sister show target cells in peripheral blood, two other children and the mother normal.

This case was thought to be a mild variety of Cooley's anæmia, as found in heterozygous children. After iron therapy for six months the Hb is 64%.

Dr. Arnold H. Banton (*in absentia*) said that although rare in Europe the disease was relatively common in Cyprus. He had recently conducted an investigation of the condition among Cypriots in their native land, the results of which he hoped would shortly be published.

It was important to differentiate between the "trait" and the disease. He found the trait exhibited by about 20% of the Cypriot population, a figure which agrees fairly closely with Fawdry's findings. The essential features of the trait were a normal hemoglobin, but the blood picture may show anisocytosis, poikilocytosis and usually "target" cells, and increased resistance to hypotonic saline. It is believed that the trait is inherited not as a Mendelian dominant, as was formerly supposed, but as an abnormal recessive.

The fully fledged disease usually occurs in the children of parents both of whom show the trait, but not all the children of such a union are necessarily affected.

Dr. Banton mentioned two clinical features which he had observed: (1) premature closure of the fontanelle; and (2) ulceration of the shins, recurrent and slow in healing. This last was not distinctive of Cooley's anæmia but occurred in other chronic hemolytic anæmia such as acholuric jaundice. Bone changes were seldom seen in those who exhibited the trait only.

Giant Hypertrophic Gastritis.—W. A. BOURNE, M.D., and W. R. FORRESTER WOOD, F.R.C.S.

Male, lorry driver, aged 27, admitted to the Royal Sussex County Hospital with a month's history of progressive loss of weight, increasing dyspnoea, oedema of ankles, and vague dyspeptic symptoms, dating from a brief attack five months before admission of epigastric pain one hour after food, with nausea. Since then the appetite had been poor. For five months there had been increasing palpitation, lassitude and pallor.

Past history of appendicectomy and peritonitis, 1937; malaria 1943; and mild attacks of diarrhoea at that time.

Family history.—Mother's death at 44 from "heart failure"; nothing otherwise notable. Tobacco consumption, 20 cigarettes daily; alcohol consumption very small.

Clinically there was pallor, oedema of ankles and over sacrum, rhonchi and râles at the right lung base; and, except for a paramedian scar, no abdominal abnormality.

Special investigations.—Blood: R.B.C. 2,900,000; Hb 26%; C.I. 0.46 (the red cells showed marked hypochromasia and polychromasia with poikilocytes, microcytes and a few monocytes); W.B.C. 10,300 (neutros. 52%, lymphos. 43%, eosinos. 1%, monos. 4%). Fragility, clotting and bleeding time normal. W.R. (blood) negative. No malarial parasites seen. No occult blood in one specimen of faeces. Histamine test meal within normal limits, maximum free acidity 50%. *Entamoeba histolytica* in vegetative and encysted forms in stools. Barium meal, multiple filling defects along the whole of the greater curve. Gastroscopy, large nodular protuberances covered by reddened mucosa.

Section of Medicine

President—MAURICE DAVIDSON, M.D.

[October 28, 1947]

DISCUSSION ON CHEMOTHERAPY IN MALIGNANT DISEASE

Professor Alexander Haddow: Although the need for an efficient chemotherapy is measured by the limitations of surgery and radiotherapy, the student of cancer cannot but be impressed—since he is best qualified to judge them—by the manifold difficulties which the subject presents. The main difficulties arise from the fact that the cancer cell is but a modification of the normal, that conversion to malignancy may be due to a re-orientation of enzyme constitution quite unaccompanied by any gross changes affecting protein structure or immunological specificity, that there is on this account no protective reaction on the part of the body such as occurs in infections, and that the malignant state appears highly stable, if not irreversible. It seems probable that the normal and malignant stages are separated by an energy barrier, and the ideal chemotherapy, that is the re-conversion from malignant to normal, would hence demand the application to the malignant cell of an amount of energy probably greater than that required for the original conversion, and in a way which is quite beyond our powers at the moment. Apart from this ultimate objective, we are nevertheless already able to achieve useful if limited therapeutic effects by other means, as in the treatment of carcinoma of the prostate with œstrogens, and through the action of the chloroethylamines in Hodgkin's disease and of urethane in leukæmia. It is not without interest that all these developments have arisen entirely naturally, through the pursuit of observations either incidentally or for their own sake, and without any immediate thought of practical application.

I was particularly struck by this in a recent discussion with Dr. Charles Huggins in Chicago, when he described to me the influence upon later work of his early experience at the Lister Institute, working with Robison on phosphatases. So, too, it is well known how the cytotoxic effects of the chloroethylamines, on tissues in a state of active proliferation, were recognized from chemical warfare studies of the nitrogen analogues of mustard gas (*see* A. Gilman and F. S. Philips, *Science*, 1946, 103, 409). In discussion of a recent paper by J. F. Wilkinson and F. Fletcher (*Lancet*, 1947 (ii), 540), on alkylamines in the treatment of leukæmia and Hodgkin's disease, Dr. Ff. Roberts is of the opinion (*Lancet*, 1947 (ii), 634) that these agents have little future, and that they may prove a disastrous failure as compared with radiation. It may, however, be that practical assay and comparison are not important at this early stage, and certainly our attention should not be deflected from effects which are, as experiment shows, of remarkable interest in themselves. A similar situation is found in the case of urethane. Following early accounts of phenyl urethane as a mitotic poison, Templeman and Sexton had studied the effects of various arylcarbamic esters on cereals and other plant species, when the production by several of these agents of characteristic effects on nuclear division, with resulting inhibition of growth, led to their use in the elimination of graminaceous weeds. Similar work in animals (Haddow and Sexton, *Nature*, 1946, 157, 500), led to the discovery that urethane itself can be regarded as a mitotic poison and produces inhibitory effects upon the growth of various animal tumours. Then followed a clinical trial which was largely negative until the further discovery of the radiomimetic action of urethane in leukæmia (Paterson, Ap Thomas, Haddow and Watkinson, *Lancet*, 1946 (i), 677).

All these developments are of interest and promise, and it must therefore continue to be our duty to encourage the study of what for want of a better term we may call the chemotherapy of cancer.

On examination he was pale and had slight but definite icterus; the spleen was enlarged 1½ in. below the level of the umbilicus; the liver was not enlarged; lymph glands were readily palpable but not definitely enlarged. 18.4.47: Hb 43%; R.B.C. 2,050,000; nucleated cells 28,000; polys. 23%; myelocytes and metamyelocytes 12%; myeloblasts 9%; normoblasts 30%; monos. 3%; lymphos. 20%; lymphoblasts 3%. (This leuco-erythroblastic reaction has been seen in all subsequent counts.) 19.4.47: Serum bilirubin 1.5 mg.%; 27.4.47: Reticulocytes 4.2%; Hb 50%; R.B.C. 2,820,000; packed cell volume 24.5%; mean corpuscular volume 8.7 cu. μ ; mean corpuscular Hb concentration 28%; mean corpuscular diameter 7.2 μ . Subsequent investigations.—W.R. negative, fragility R.B.C. normal, Bence-Jones protein absent, sternal puncture failed twice, bleeding and coagulation times normal. X-ray of bones—multiple punched-out areas of infiltration bone and bone-marrow (fig. 1). 3.6.47: Biopsy of deposit in right femur (Mr. Hedley Hall), white fibrous nodule lifted out of cavity in *corticalis*. Histological examination (Dr. J. F. Heggie) revealed "fibrocellular-osteoid combination which shows osteoclastic activity and fibrous replacement of the bony trabeculae most of which show resorption of calcium salts and have reached osteoid state" (fig. 2).

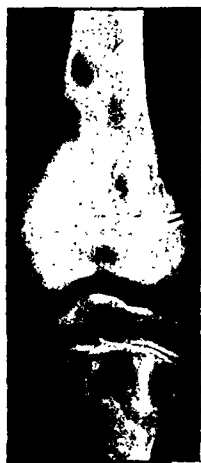


FIG. 1.—F. B. X-ray of right femur.



FIG. 2.—F. B. Section of fibrous nodule in bone ($\times 135$).

(Photographs by E. W. Hall, A.R.P.S.)

Progress and treatment.—Icterus disappeared within a few days of admission. Given blood transfusions and iron. Hb rose steadily to 80%. Low fever present throughout admission. 14.7.47: Hb 68%. Testosterone propionate—5 mg. twice a week—started 15.7.47. 5.9.47: Hb 72%; R.B.C. 4,020,000; nucleated cells 57,000; polys. 7%, myelocytes and metamyelocytes 57%, myeloblasts 25%, lymphos. 4%, lymphoblasts less than 1%, monoblasts less than 1%, erythroblasts 5%, platelets 278,000. The spleen is now grossly enlarged coming to within 1 in. of the right superior iliac spine.

Dr. C. J. C. Britton has suggested a diagnosis of myelosclerosis in this case.

Dr. F. Parkes Weber said that the skiagrams of the long bones made him think of what he would call "Polyostotic focal fibrous dysplasia" (not connected with hyperparathyroidism), but he had never heard of this condition being accompanied by a blood picture of leuco-erythroblastic anaemia.

Dr. Herbert Levy agreed that this was a case of myelosclerosis. The suggestion of polyostotic fibrous dysplasia could not be upheld as that condition never leads to leuco-erythroblastic anaemia and splenomegaly; moreover, in contrast to the present case, the bony lesions tend to be unilateral and show histologically minimal osteoclastic resorption. He also agreed that there was good reason to adhere to the view that the splenic enlargement is compensatory and that splenectomy cannot therefore be contemplated.

mitosis has been obtained with both materials which resembles that of X-rays and differs from that of colchicine in that no effect on the spindle has been observed.

Spores soaked for six hours in 0.5% urethane show less effect than if given 1,000 r X-rays; fibroblasts soaked for twenty-four hours in a 0.1% concentration show similar effects to those given 30 r X-rays. In tissue cultures no augmentation of effect has been found by combining urethane and X-rays, the effect of X-rays being lessened if urethane is administered after radiation. In fern spores this lessened effect of radiation is also obtained if urethane is administered first, but not when given after irradiation. So far the work shows that urethane acts directly on the cell; that mitosis is inhibited and differentiation is induced. The similarity of urethane and X-ray effects suggests the possibility that urethane may be also capable of inducing changes in chromosomes.

Dr. Inez Ap Thomas: Nitrogen mustard therapy.—The following is a summary of our results of treatment with nitrogen mustard. The compound used in most cases was methyl-bis (B-chloroethyl) amine hydrochloride. Only a few received tris (B-chloroethyl) amine hydrochloride. The total number treated is 41. 27 of these were cases of Hodgkin's disease, proved by section. The treatment is not curative, and the aim is to produce symptomatic improvement.

A summary of the improvement is shown in Tables I and II.

TABLE I.—RESULTS OF FIRST COURSE OF NITROGEN MUSTARD TREATMENT IN 27 CASES OF HODGKIN'S DISEASE.

Sign or symptom	Total	Improved	% improved
Enlarged nodes	23	21	92
Enlarged mediastinum	7	7	100
Enlarged abdomen	7	7	100
Enlarged spleen	4	4	100
Poor general condition.. ..	18	18	100
Pyrexia	13	10	77
Skin rash	2	2	100
Pain	5	5	100
C.N.S. involvement	1	0	0

TABLE II.—PERCENTAGE IMPROVEMENT IN ALL SYMPTOMS IN PATIENTS UNDER NITROGEN MUSTARD TREATMENT

1st course 27 cases	2nd course 16 cases	3rd course 8 cases	4th course 1 case	fortnightly 3 cases
92%	73%	60%	100%	100%

Improvement was not maintained, but the patient improved again with further treatment. The total dose in most cases was 0.4 mg./kg. of body-weight in two days (two injections) for the first course. In later courses this was increased to 0.6 mg./kg. in two days. Later courses were given of 0.1 mg./kg. at fortnightly intervals.

Leucopenia followed treatment but this was temporary. It was occasionally serious as in one case treated with tris (B-chloroethyl) amine hydrochloride, where the total white blood-count fell to 200, the hæmoglobin to 40% and platelets to about 11,000. Several blood transfusions were necessary for recovery.

In our series other reticuloses and malignant tumours did not respond well, though carcinoma lung did improve temporarily.

The report is a confirmation that the nitrogen mustards are of value in Hodgkin's disease when radiation treatment is not practicable, but that they should not be used as an alternative to X-ray therapy in early cases, since the remissions with nitrogen mustard are shorter and the toxic effects more severe.

Mr. E. W. Riches (Middlesex Hospital): My remarks will be confined to the use of synthetic oestrogens in the treatment of carcinoma of the prostate. In this disease there is no doubt that such treatment is beneficial and the immediate results are

Dr. Edith Paterson: *Urethane in leukaemia.*—The previous work done on the effect of urethane in leukaemia has been extended and information has been gained on the effect of urethane on cells.

No beneficial effect has been obtained in acute or terminal cases of leukaemia, although in the former a very temporary improvement in the blood occurs. In chronic leukaemia the results have been good both in improving the general condition of the patient and in altering the blood towards the normal. This improvement is indistinguishable from that which follows the usual method of treatment by splenic irradiation.

In the myeloid type the white cell count has fallen in every case. Typically the reduction in white cells is accompanied by a rise in hæmoglobin, and the differential count also approaches normal. In most cases the myeloblasts disappeared. In a few patients a rise in metamyelocytes occurred at the expense of a decrease of more primitive forms. This suggests that one effect of urethane is to promote differentiation.

The rise in red cells coincides with the diminution of a high white cell count. The amount of the rise is important in assessing the prognosis. About half of the cases showed an immediate rise in hæmoglobin which exceeded 10%; the remainder showed a lesser rise, or fell. In the former group the expectation of life has been more than twice that in the latter group. The effect of urethane on the platelet count was parallel to that on the red cells. A low platelet count rose; a high platelet count either remained stationary or rose. The bone-marrow responded similarly to peripheral blood; erythropoiesis increased with a diminution of myeloid cells. As with X-ray therapy the spleen diminished in size in every case and in some instances became impalpable.

In chronic lymphatic leukaemia the effects are similar, but differences exist. The white cell count falls, but probably with less constancy than in myeloid leukaemia. The differential count improves; the polymorphs increase and lymphoblasts tend to disappear. The hæmoglobin rises after treatment, but unlike myeloid leukaemia the rise does not bear a clear relationship to prognosis. A low platelet count is a usual finding in these cases; after treatment this either rose or remained stationary. No parallelism was found between the rise in hæmoglobin and the effect on the platelets. As with myeloid leukaemia the marrow in lymphatic leukaemia showed an increase in the proportion of nucleated red cells. Since this occurred even when the peripheral red cell count was satisfactory, it illustrates the need for examination of the marrow in lymphatic leukaemia before judging suitability for treatment. Diminution in the size of the spleen and lymph nodes was less constant than in myeloid leukaemia.

Experience has shown that urethane can be regarded as an alternative to X-ray treatment in leukaemia. As with X-rays, the urethane treatment of leukaemia may present difficulties. Nausea occurs in some cases, but in these the drug may be given in capsule form, or rectally in saline. The intravenous method used by Storti and Mauri has also been found useful. An excessive dose of urethane may result in aplasia of the bone-marrow with leukopenia and a fall in hæmoglobin and in platelets.

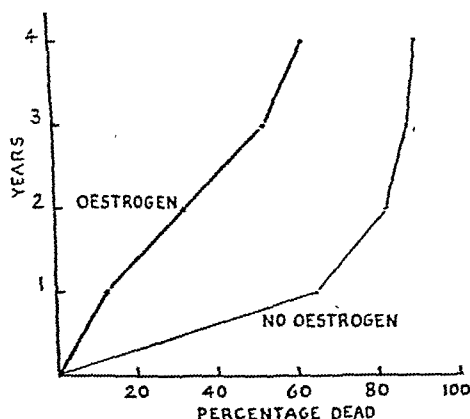
Post-mortem examinations have been carried out in a number of urethane treated cases, and the findings compared with those of a similar sample of patients treated by X-rays. The causes of death were the same in the two groups; about one-third of the patients died of infection, including tubercle; the remainder died of the usual sequels of leukaemia. Two cases treated by urethane showed a moderate degree of fibrosis of the marrow. Another showed excessive organization of old pneumonic areas. It is uncertain whether either of these changes is a specific effect of urethane.

Experimental work has been carried out on the effect of urethane on normal and malignant cells and the combined effect of urethane and X-rays. Spontaneous mammary tumours in mice show a temporary regression. The effect on normal cells has been tested on fern spores and on fibroblasts *in vitro*. An inhibition of

in the expectation of life and in particular to reduce the alarming mortality of the first year.

Dosage.—It is my practice to start with 1 mg. of stilbœstrol t.d.s. and increase the dose daily by 1 mg. t.d.s. up to 5 mg. t.d.s. The patient remains on 15 mg. daily for a variable number of weeks or months; occasionally 20 mg. daily is given. Provided that the serum acid phosphatase remains normal the dose is gradually reduced. The adequate maintenance dose is assessed by the general and local condition and by the level of serum acid phosphatase. It is never less than 1 mg. daily and may remain at 15 mg. daily. In a very few cases stilbœstrol has produced nausea or vomiting and dienœstrol has been substituted but my impression is that it is less effective than stilbœstrol. However, I have one patient surviving four years and five months who has taken dienœstrol throughout.

The value of the serum acid phosphatase is variable, but I consider that it should be estimated before any œstrogen is given. If raised, as when osseous metastases are present, its subsequent fall is an index of response and a guide to the correct maintenance dose. If the dose is inadequate the acid phosphatase rises again, and this may be an indication of further metastases (graph 2).



GRAPH 1.—Carcinoma of the prostate. Percentage dying each year up to four years.

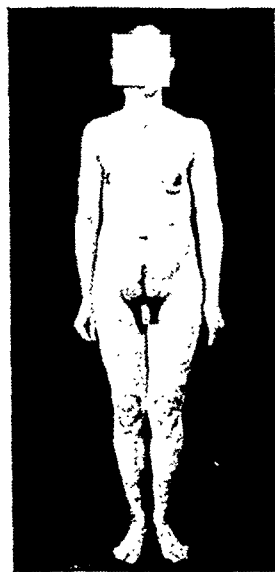
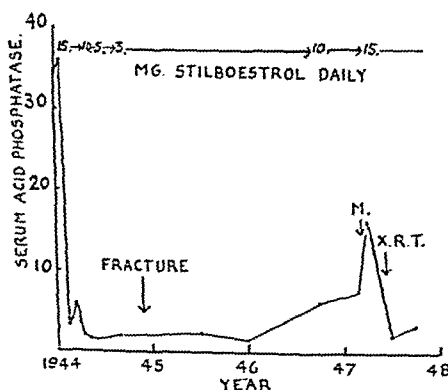


FIG. 1.—Enlargement of breasts, pigmentation of nipples and of abdominal scar produced by œstrogens.



GRAPH 2.—Level of serum acid phosphatase in a case of carcinoma of the prostate with osseous metastases. M—New metastasis discovered. X R T — X-ray therapy.



FIG. 2.—Pigmentation of nipple produced by œstrogens.

well known. There are, however, differences of opinion on the number who respond, the duration of the benefit, the proper dosage, and the general management of a case including the need for adjuvant surgical treatment. In order to try and answer these questions I have reviewed all my cases treated for a minimum of three years. I started using stilbæstrol early in 1943, stimulated by a paper by Professor Haddow read at the Faculty of Radiologists (1943).

There are 16 cases treated for four years and upwards, and 24 treated for three years and upwards, a total of 40. At the same meeting I reported on 70 cases treated before stilbæstrol came into use so that I have figures for comparison (Riches, 1943). In 37 of the 40 the diagnosis has been verified histologically, and in the other 3 by the presence of osseous metastases, and a high acid phosphatase.

There are two clinical varieties of carcinoma of the prostate, the primary scirrhus and the adenocarcinoma arising secondarily in a gland which is the seat of benign hypertrophy. The former usually starts in the posterior lobe and is easily recognized as being malignant from the outset. It occurs at a younger age than the adenocarcinoma, and is more lethal. The secondary type may not be discovered until the gland is examined microscopically after its removal for benign hypertrophy, and the patient may then live for ten years or more without other treatment before getting a recurrence. Complete cure is only likely in this type, and it will naturally give better statistical results after stilbæstrol just as after any other method of treatment. Unfortunately there is no marked histological difference between the two, and the distinction is purely clinical. Hence most statistics group them both together and this renders the assessment of results of treatment open to misinterpretation.

Pre-æstrogen results.—The average five-year survival rate before stilbæstrol was about 7% from all methods of treatment.

After endoscopic resection and X-ray therapy the average duration of life was about two years; after prostatectomy and X-ray therapy it was rather more than three years, but this group included more of the adenomatous type previously mentioned. With no treatment other than permanent suprapubic cystostomy the average was nine months.

Failure to respond.—If we now consider the 40 cases in which æstrogens have been used for four and three years the number who failed to respond was 3, or 7.5%. One of these lived three months, one five months, and one two years and three months, but the growth showed no sign of regression.

Duration of benefit.—The number alive at the end of each year is shown in Table I.

TABLE I.—ÆSTROGEN TREATMENT 1943 AND 1944: TOTAL 40

Alive after 1 year	..	35	87.5%	Alive after 3 years	..	19	47.5%
Alive after 2 years	..	29	72.5%	Alive after 4 years	..	6	15%

(Two cases are untraced after six weeks and two years respectively, and these are presumed to have died at those times.)

Percentages in such small numbers are scarcely justifiable, and it must be remembered that 16 of those in the three and four year groups are still alive. Analysis of the four-year group separately gives the following figures.

TABLE II.—ÆSTROGEN TREATMENT FOUR OR MORE YEARS: TOTAL 16

Alive (October 1947)	5	31%
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Figures of four-year survivals before the use of æstrogens were given by Harnett (1944) for a total of 382 cases; 90% were dead after four years. They are plotted in graph 1 together with the present series of 40 cases to show the percentage dying at the end of each year. The use of stilbæstrol appears to give a significant increase

clinical grounds. Such treatment "in the dark" frequently delays the correction of benign prostatic obstruction and is apt to bring a valuable method into disrepute.

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Dr. E. Boyland (*Chester Beatty Research Institute, The Royal Cancer Hospital (Free)*): At the present time workers on the chemotherapy of cancer are concerned with palliative drugs, which inhibit the growth and spread of tumours but do not destroy them. That these inhibiting agents are themselves carcinogens appears superficially as a remarkable paradox in our present knowledge of the subject. That ionizing radiations have beneficial effects in cancer and can induce cancer has been known for many years. Other examples of agents with the two actions include the oestrogens which are effective in treatment of cancer of the prostate and induce cancer of the mammary gland and other organs, urethane which controls chronic leukaemia and induces cancer of the lung in animals, and 4-dimethylaminostilbene which inhibits the growth of tumours and induces cancer at many different sites in animals.

The close relation between carcinogenesis and inhibition of growth and the use of carcinogens in chemotherapy means that the study of the mechanism of action of carcinogens has a twofold interest, first for its own sake, leading possibly to prevention of the disease, and secondly for the study of the inhibitory actions which might help in the discovery of new chemotherapeutic agents.

The determination of the optimum or even adequate dosage in cancer chemotherapy is difficult but most important. The dosage schedule is very critical in treatment with nitrogen mustard. When mice with spontaneous mammary tumours or with transplanted lymphosarcomata were treated with four daily doses of 0.1 mg. per kg. of tris (B-chloroethyl) amine hydrochloride no inhibition of growth or prolongation of life was produced. When the same drug, however, was given as a single dose of 0.4 mg. per kg., inhibition of growth and prolongation of life were observed.

A remarkable feature of the chloroethylamines is the similarity of their action to the action of ionizing radiations. This is seen in the effect on the nuclei where chromosome fragmentation and increased stickiness of chromosomes may result. Both chloroethylamines and radiations can cause vesication, nausea, vomiting, leucopenia and thrombocytopenia.

In clinical trials chloroethylamines have produced better palliative effects in cases of Hodgkin's disease and in bronchogenic carcinoma than in cases of other forms of carcinoma. Such preferential action is common among these agents, as shown in the use of oestrogens for prostatic cancer and urethane for leukaemia. A pessimistic view of chemotherapy of cancer is that cancer cells are so similar to normal cells that no agent differentiating between them will be found. But if a compound is effective against one type of tumour only, then it is less likely to damage other normal organs. Because of this specificity of action in the existing agents, a range of different types of animal tumours should be used in the search for new drugs. Each new compound might be tested against a variety of forms of malignant disease including leukaemia, cancer of the mammary gland, prostate, lung, stomach, liver and bone. One striking indication of the progress which has been made in the subject is that prolongation of life can often be used as the criterion of effectiveness. We have substances such as the chloroethylamines, urethane and aminostilbenes which will prolong life of cancerous animals, and such compounds can be used as standards against which new substances can be compared.

The most important aspect of dosage is that the prescribed œstrogen must be taken regularly and continuously for the rest of the man's life. This must be impressed upon him, and his doctor. I have only too frequently seen its discontinuance for some slight side-effect followed by a reactivation of the disease.

General management.—90% of patients with carcinoma of the prostate have some degree of urinary obstruction, and the sooner it is relieved the better the outlook. Whilst stilbæstrol will often give this relief the process is a slow one; and surgical treatment is preferable. The most useful form for this disease is endoscopic resection of the prostate which not only overcomes the urinary obstruction, but provides material for biopsy. I have found adjuvant surgical treatment necessary in 36 of these cases (Table III).

Metastases.—Metastases were present at some stage in more than half the cases (Table IV).

TABLE III.—ADJUVANT SURGICAL TREATMENT

Endoscopic resection ..	27
Prostatectomy ..	7
Diathermy excision ..	2
Biopsy of lymphatic gland ..	1
No operation ..	3
Total	40

TABLE IV.—40 CASES. METASTASES PRESENT IN 21

Ossæous ..	15
Lymphatic ..	5
Pulmonary ..	4
Other viscera ..	2

It is probable that pelvic lymphatics were invaded more frequently: Muir (1934) showed from autopsy findings that they occurred in 77% of cases.

Secondary deposits in bone provide a good picture of the regression of the growth under œstrogens. In the patient whose phosphatase curve is shown (graph 2) metastases around the left acetabulum and in the ischiopubic rami showed considerable regression after ten months and almost complete disappearance after two and a half years. The fractured neck of the right femur after eleven months was not through a secondary deposit, but after three and a quarter years an osteolytic deposit appeared near the right acetabulum. This has again regressed under X-ray treatment and increased dosage of stilbæstrol, and he is well and walking three years and ten months after starting treatment.

Metastases in the lungs may disappear more rapidly. I have seen them disappear in three cases and I look on their occurrence as an indication for increasing the dose of œstrogen and not necessarily as a sign of impending death.

Lymphatic metastases will also regress in some cases.

Side-effects.—Testicular atrophy and cessation of erections are inevitable sequelæ of treatment. Enlargement of the breasts (figs. 1 and 2) and pigmentation of the nipples and of any scars, and of the mid-scrotal line occur in most cases. When the dose can safely be reduced the pigmented epithelium desquamates leaving a more normal coloration. These side-effects must not be taken as an indication to stop treatment.

Summary.—Carcinoma of the prostate is a disease which takes a variable course according to its clinical type. Before the use of œstrogens, however, it could be said with some certainty that the appearance of metastases usually meant death within a few months. With œstrogens this is not so and some patients may live for four years even with metastases. The most striking results are therefore seen in the worst cases, but the greatest prolongation of life follows its use in cases which have not metastasized.

It remains a surgical complaint and some form of surgery is needed in the majority of cases to get the best results. This should include the provision of material for histological examination without which treatment is often carried out on inadequate

literature on the subject which has been well summarized by Rhodes (1947). Susceptibility has also been the subject of consideration by many writers. Vitamin and œstrogenic deficiencies have been postulated, but the subject is complicated, chiefly by the fact that while infection is widespread, frank clinical disease is rare. Indeed Casey (1946) believes that perhaps "98% of poliomyelitis is a mild, widespread, highly communicable disease of young children leaving no residual paralysis".

There has always been a reservoir of poliomyelitis infection in London with sporadic cases occurring throughout the year and a generalized rise in incidence during the early summer persisting to the late autumn. In the pre-1947 pattern the peak was normally reached about mid-September and most of the annual cases occurred between the beginning of July and the end of November. Such a "peak", however, merely implied three or four cases a week instead of one a fortnight.

In London in 1947, up to October 25, 908 notifications were received, more than had previously been received in the whole decade 1937-46, and far exceeding the previous highest annual total of 134 in 1938. From the national point of view the epidemic rise was first distinguishable in the week ended May 31, when the cases reported rose by one-half (21 against 14). In London there was an apparently local beginning confined largely to the south-eastern sector which was soon overwhelmed in significance by a general and simultaneous rise in incidence throughout the county which was far too widespread to be accounted for by reference to any local beginning. It is in fact a mere academic point as to where in London the "explosion" was touched off.

In the age-analysis of the cases up to October 25, 1947, it was demonstrated that, whereas in 1937-46 the disease attacked mostly children (78% of the 1937-46 cases were under 15), in 1947 the percentage was only 64. Sex incidence in the 1947 epidemic is shown in Table I.

TABLE I.—AGE AND SEX INCIDENCE

Age	Males	Females	Age	Males	Females	Male excess
0-14	350	234	0-	21	13	+ 9
15-34	122	147	1-	32	26	+ 6
35+	28	27	2-	3	29	+ .
			3-	23	20	+ 3
	500	408	4-	33	18	+15
			5-	32	27	+ 5
			6-	29	16	+13
			7-	25	16	+ 9
			8-	16	12	+ 4
			9-	28	10	+18
			10-12	52	36	+16
			13-14	25	11	+14
				350	234	+116

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The areas of high incidence are surrounded by boroughs in which the incidence was close to the average for London as a whole, and are those clearly marked out as "isolated" areas of high incidence. What possible reasons are there for these divergencies from the average for London as a whole? Possible suggestions are:

[November 25, 1947]

Acute Anterior Poliomyelitis in 1947 with Special Reference to London

By Sir ALLEN DALEY

Medical Officer of Health, London County Council

THE 1947 outbreak of poliomyelitis in England was by far the largest that this country has ever experienced. Epidemics have been common and widespread in North America, Scandinavia, Australasia, and, during the recent war, in the islands of Malta, Mauritius and St. Helena. These island outbreaks are of particular interest and we shall return to them later on.

My own interest in the subject was stimulated in 1927 when an outbreak occurred in the City of Hull of which I was then Medical Officer of Health (Daley, 1927). A similar outbreak had occurred the previous year in Leicester and another in the following year in Glasgow, but, apart from these, the country as a whole had been remarkably free. There was nothing of special note in Leicester, Hull or Glasgow in any of these years and why it should have spread there and nowhere else is one of the mysteries of epidemiology.

It is pertinent first of all to discuss the value of notifications as an index to the incidence of the disease. Some decry them as valueless because the vast majority of poliomyelitis infections are so mild that they pass unnoticed, whereas when there is a local scare these, and many other illnesses, are notified as poliomyelitis. This is a valid criticism, but it is clear that cases developing paralysis are never likely to escape notification, and that, judged by paralytic cases, epidemics have occurred, the stature of which can roughly be assessed by the notification rates. When the disease is receiving widespread publicity, comparisons of incidence in one part of the country and another on a basis of notifications are reasonably valid, for the factor of error is likely to be of a comparable order throughout.

Assuming, therefore, notifications to be a rough guide to incidence, the most interesting features in recent years here and in North America are (i) a shift in the age-incidence towards the older age-groups and (ii) an increase in the number of cases of the brain-stem type. It is stated that in Japan, among the native population, there are sporadic cases with occasional epidemics involving children under two years (Van Riper, 1947), but although Japanese adults rarely develop the disease, American adults in the Army of Occupation do so. Burnet (1945) believes that more people now reach adolescent or adult life without developing immunity because modern sanitation has reduced the likelihood of subclinical infection from alimentary sources in childhood. This theory receives support from the aforementioned island outbreaks where the standards of sanitation are not high. For whereas in Malta (Agius, 1945; Bernard, 1945; Debono, 1945; Seddon *et al.*, 1946) and Mauritius (McFarlan, 1946; McFarlan, Dick and Seddon, 1946) where the disease is endemic, the majority of cases occurred in children under 5 years, in St. Helena (Kauntze, 1946) where the disease was previously unknown, the children under 5 were little affected and most cases occurred in the age-group 10-25. All three epidemics are believed to have been introduced by the armed forces of the Allies. The adult is more likely to develop the brain-stem form than the infant, hence Burnet's theory would explain both the higher age-incidence and the increase in bulbar palsies.

The number of suggested vehicles of infection is legion, but modern opinion has narrowed the issue down to two—both deriving from the human case or carrier—droplet spread from the nasopharynx or spread from the excreta through the familiar mechanism of "fingers, food and flies". Space forbids a review of the immense

literature on the subject which has been well summarized by Rhodes (1947). Susceptibility has also been the subject of consideration by many writers. Vitamin and æstrogenic deficiencies have been postulated, but the subject is complicated, chiefly by the fact that while infection is widespread, frank clinical disease is rare. Indeed Casey (1946) believes that perhaps "98% of poliomyelitis is a mild, widespread, highly communicable disease of young children leaving no residual paralysis".

There has always been a reservoir of poliomyelitis infection in London with sporadic cases occurring throughout the year and a generalized rise in incidence during the early summer persisting to the late autumn. In the pre-1947 pattern the peak was normally reached about mid-September and most of the annual cases occurred between the beginning of July and the end of November. Such a "peak", however, merely implied three or four cases a week instead of one a fortnight.

In London in 1947, up to October 25, 908 notifications were received, more than had previously been received in the whole decade 1937-46, and far exceeding the previous highest annual total of 134 in 1938. From the national point of view the epidemic rise was first distinguishable in the week ended May 31, when the cases reported rose by one-half (21 against 14). In London there was an apparently local beginning confined largely to the south-eastern sector which was soon overwhelmed in significance by a general and simultaneous rise in incidence throughout the county which was far too widespread to be accounted for by reference to any local beginning. It is in fact a mere academic point as to where in London the "explosion" was touched off.

In the age-analysis of the cases up to October 25, 1947, it was demonstrated that, whereas in 1937-46 the disease attacked mostly children (78% of the 1937-46 cases were under 15), in 1947 the percentage was only 64. Sex incidence in the 1947 epidemic is shown in Table I.

TABLE I.—AGE AND SEX INCIDENCE

Age	Males	Females	Age	Males	Females	Male excess
0-14	350	234	0-	21	13	+ 9
15-34	122	147	1-	32	26	+ 6
35+	28	27	2-	3	29	+ .
			3-	23	20	+ 3
	500	408	4-	33	18	+15
			5-	32	27	+ 5
			6-	29	16	+13
			7-	25	16	+ 9
			8-	16	12	+ 4
			9-	28	10	+18
			10-12	52	36	+16
			13-14	25	11	+14
				350	234	+116

In a summary of 36,000 cases (mainly American) of all ages, the International Committee found in 1932 that the male to female ratio was 1.3 : 1. The comparative overall ratio in London was 1.23 : 1.

Table II compares the incidence in each Metropolitan Borough. Fig. 1 shows the geographical distribution of individual cases represented by spots on the map.

Several features emerge. The boroughs with a significantly higher-than-average notification rate are Chelsea, Shoreditch, Southwark, Bermondsey and Lewisham. The experience of Islington is noteworthy. Not only did this borough have a significantly lower-than-average incidence, but those cases which did occur were crowded towards the Shoreditch boundary.

The areas of high incidence are surrounded by boroughs in which the incidence was close to the average for London as a whole, and are those clearly marked out as "isolated" areas of high incidence. What possible reasons are there for these divergencies from the average for London as a whole? Possible suggestions are:

TABLE II.—ATTACK RATES IN METROPOLITAN BOROUGHES

	Population 30.6.47	Notifications of P.M. and P.E. (1.1.47 to 27.10.47)	Attack rate per 1,000 living (1.1.47 to 27.10.47)	Expected cases and standard error	Difference of actual and expected cases	Significant on 5% level
Paddington ..	127,920	22	0.172	34.9± 5.9	-12.9	*
Kensington ..	167,610	25	0.149	45.7± 6.8	-20.7	*
Hammersmith ..	118,040	32	0.271	32.2± 5.7	- 0.2	
Fulham ..	123,040	35	0.284	33.6± 5.8	+ 1.4	
Chelsea ..	51,690	24	0.464	14.1± 3.8	+ 9.9	*
Westminster, City of ..	103,430	21	0.203	28.2± 5.3	- 7.2	
St. Marylebone..	77,260	16	0.207	21.1± 4.6	- 5.1	
Hampstead ..	95,750	14	0.146	26.1± 5.1	-12.1	*
St. Pancras ..	137,150	31	0.226	37.4± 6.1	- 6.4	
Islington ..	238,630	28	0.117	65.1± 8.1	-37.1	*
Stoke Newington	46,200	11	0.238	12.6± 3.5	- 1.6	
Hackney ..	175,670	54	0.307	47.9± 6.9	+ 6.1	
Holborn ..	23,680	9	0.380	6.5± 2.5	+ 2.5	
Finsbury ..	35,260	10	0.284	9.6± 3.1	+ 0.4	
City of London	5,490	—	—	1.5± 1.2	- 1.5	
Shoreditch ..	44,960	44	0.979	12.3± 3.5	+31.7	*
Bethnal Green ..	60,320	22	0.365	16.5± 4.1	+ 5.5	
Stepney ..	100,450	30	0.299	27.4± 5.2	+ 2.6	
Poplar ..	74,050	13	0.176	20.2± 4.5	- 7.2	
Southwark ..	92,590	37	0.400	25.3± 5.0	+11.7	*
Bermondsey ..	59,340	25	0.421	16.2± 4.0	+ 8.8	*
Lambeth ..	224,890	48	0.213	61.3± 7.8	-13.3	
Battersea ..	115,650	29	0.251	31.5± 5.6	- 2.5	
Wandsworth ..	332,650	92	0.277	90.7± 9.5	+ 1.3	
Camberwell ..	175,920	49	0.279	48.0± 6.9	+ 1.0	
Deptford ..	73,710	20	0.271	20.1± 4.5	- 0.1	
Greenwich ..	83,060	24	0.289	22.7± 4.8	+ 1.3	
Lewisham ..	223,220	111	0.497	60.9± 7.8	+50.1	*
Woolwich ..	140,710	32	0.227	38.4± 6.2	- 6.4	
London County	3,328,340	908	0.2728	908.0±30.1	—	

(a) *More complete notification or over-notification.*—Frank cases of paralysis can hardly have escaped notification anywhere. On the other hand many patients were admitted to hospital as suspected poliomyelitis in whom the diagnosis was not confirmed. For patients treated in L.C.C. hospitals up to the end of August the proportion not confirmed was 43% but there is no evidence that such errors of diagnosis were more common in one borough than another.

(b) *Social conditions.*—To test the relationship of incidence with social conditions an examination has been made of the correlation of poliomyelitis attack rate with the social index of the boroughs, i.e. the proportion of males aged 14+ who were in social groups IV and V (the lowest groups financially) at the 1931 census. No significant association was found.

(c) *Differences in immunity level.*—We know so little about this that it is impossible to say whether or not there were any differences between the different boroughs.

(d) *Differences in methods of control.*—The methods of control which were adopted are set out later. I have personal doubts as to the real efficacy of any of these, but they were applied in every borough and I do not think that any slight differences there may have been affected the borough incidence.

Examination of the borough statistics therefore throws no light on the epidemiological factors involved.

Age-incidence.—The notifications in London since 1921 have been analysed for incidence in children under 5. The figures are shown in Table III. Between 1921–23

LONDON: ADMINISTRATIVE COUNTY.

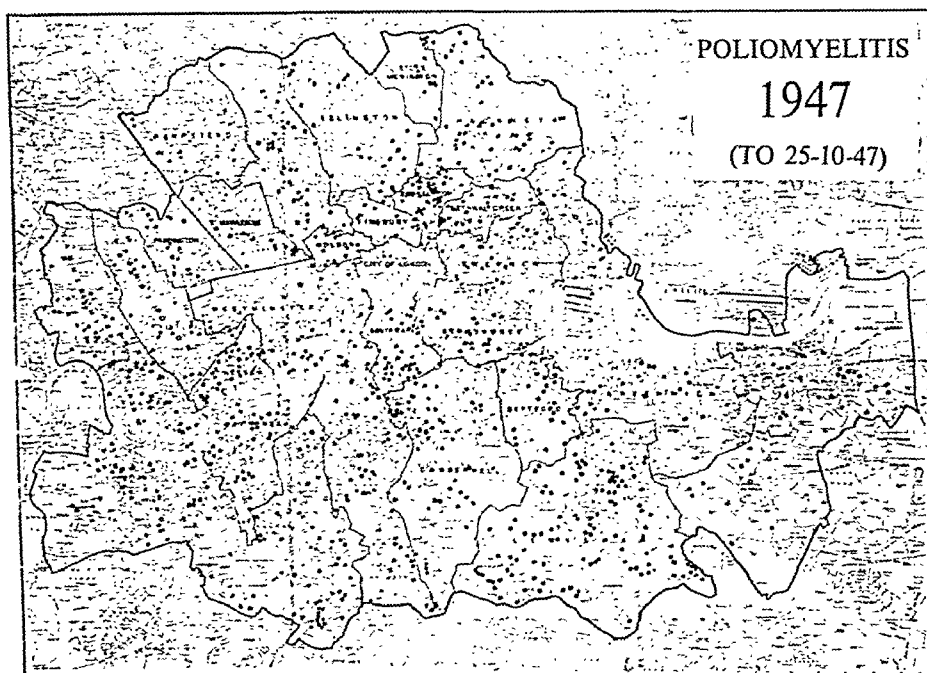


FIG. 1.

TABLE III.—NOTIFICATIONS OF POLIOMYELITIS AND
POLIO-ENCEPHALITIS

	Total No.	Under 5 years of age No.	Per cent
1921-23	209	116	55.5
1924-26	266	152	57.1
1927-29	206	117	56.8
1930-32	182	107	58.8
1933-35	225	112	49.8
1936-38	280	114	40.7
1939-41	159	72	45.3
1942-44	88	41	46.6
1945	70	22	31.4
1946	39	14	35.9
1947	908	249	27.4

and 1936-38, the proportion of the total population in the under 5 age-group fell from 8.8% to 6.1%, subsequently rising to 7.3% in 1946. The fall in the infant population might account for some of the decline from 55.5% (in 1921-23) to 40.7% (in 1936-38) and 27.4% (in 1947) in the proportion of infantile cases of poliomyelitis, but that the decline should have persisted despite the reversal of the population trend suggests either that recently there has been an increase in the number of infants who have been immunized and are therefore insusceptible to attack with a corresponding increase in the unimmunized among those who are older, or that there has been some change in the virus to which the older age-groups are now more susceptible.

Housing conditions—Overcrowding: Out of 908 notifications there were only 27 instances covering 59 cases of more than one reportable case in the same building, i.e. the risk of a multiple case is 3%. This low risk indicates either that contact is not important, or that the rest of the family are immune, or, although the whole household is infected, in one only does the virus give rise to a clinical case. It is of interest to know the periods between infection in multiple cases.

Days:	0-2	3-5	6-8	9-11	12+
Occurrence:	15	1	2	4	10

Thus if we exclude the cases notified within a few days of each other, the number of true secondary cases is very small indeed. In 23 families or communities there were 2 cases; in three, there were 3 cases; and, in one instance, there were 4 cases. Space forbids discussion of the reasons for this, but there is some statistical evidence that true paralytic poliomyelitis is less common in overcrowded households.

Contact and exposure.—The contact and exposure history of a sample of 391 hospital cases is shown in Table IV but there is little or nothing to be learned from them and no controls by which the value of the figures might be assessed.

TABLE IV.

HISTORY OF CONTACT					TABLE IV.				
At home	33	Recent visits to swimming pool ..	7						
At school	—	Tooth extractions	2						
At work	7	Tonsillectomy	6						
No history of contact	351	Violent exercise	13						
<hr/> Total cases in series		<hr/> 391							

General epidemiological considerations.—Very few lessons have emerged from our analysis. We do not know why the disease was so much more prevalent in England in 1947 than ever before. Various theories, unsupported by facts, have been put forward. The hard winter, followed by a hot, dry summer, has been blamed. This as a causal factor, is pure surmise. Others relate the epidemic to poor nutrition, but poor nutrition cannot be the cause of the epidemics in the U.S.A. or Australia which are among the best-nourished nations in the world, and neither in those countries nor in this is there any evidence that the disease picks out the undernourished. Another theory is that a variant of the virus has been introduced by the returning troops and that it has broken through the resistance of those immune to the native virus. It may well be that there is something in this theory.

Authentic cases are reported of second attacks. This may be due to the immunity being short-lived or to attack by a different type of the virus. What is the explanation of the change in the age-incidence? Assuming (a) that immunity is, in the vast majority of cases, lasting, (b) that during the course of immunization only a very small proportion of those infected develop the clinical disease, and (c) that there has been no marked change in the type of the virus, the only theory which would account for the alteration in the age distribution would be that until a decade or so ago the vast majority of the population were infected in infancy by the nasopharyngeal or alimentary route. By assumption (b) the total number of clinical cases was small but the bulk of the cases occurred among infants. The patients in those years who developed the disease at a later age had escaped immunization in infancy. The rise in the age-incidence during recent years would point to a larger proportion of the population having failed to be immunized in infancy. This may have been due, as Burnet suggests, to improved sanitation, particularly in relation to food handling.

MEASURES OF CONTROL

Obviously in dealing with a disease, the natural history of which is so imperfectly known, the task of the Health Officer who is endeavouring to control it is not an easy one. In London this responsibility is shared between the boroughs, the City and the county. All my colleagues have kindly informed me of the steps they took locally, many of which were in response to public pressure rather than the result of scientific conviction. It was generally assumed that spread was from the nasopharynx or from the alimentary tract. We advised that the assembly of young people in crowded, badly ventilated, rooms should be avoided, though we wished to interfere as little as possible with the normal life of the community. Gargles and sprays were usually discountenanced. A few medical officers asked that special children's cinema *matinées* should be discontinued. If a case occurred in a day nursery it was closed—this happened only in 7 out of 130 nurseries. Operation for the removal of tonsils and adenoids was, by common consent, suspended except in urgent cases. Paddling pools which could not be chlorinated were drained. Chlorinated swimming baths were kept open, but many swimming galas, because of the violent exertion involved, were cancelled. Special steps were taken to reduce the fly nuisance by attention to refuse containers. Holiday camps for school children in this country were not prohibited, but it was considered inadvisable to send parties of children abroad. At only one camp did any trouble develop. This held 240 secondary school children and assembled on July 25. One case occurred which was sent to hospital and the party went home on August 9, on which day a new party of 168 moved in. Of these, three developed the disease, but from the history it was clear that they had brought the infection with them. This batch of children left on August 23 when a vigorous attack was made on the camp and its surroundings with Gammexane, D.D.T. emulsion, &c., during the three days before the next party arrived. Among the 61 who turned up no case occurred. Another interesting example was that of a residential nursery (outside London) of 125 children below the age of 5 years staffed by 80 persons: 6 young adult nursery trainees developed the disease, but only one of the children was affected.

The County Council was responsible for the hospitalization of cases, but its resources soon came to an end. The voluntary hospitals, especially the teaching hospitals, were asked to help, which they willingly did. Of some 900 patients admitted to hospital approximately half went to L.C.C. and half to voluntary hospitals. The supply of respirators threatened difficulties, but with the help of the King Edward's Hospital Fund sufficient for all needs were provided.

In the hope that it might throw some light on aetiology, on the means for the detection of early cases and on the need for long-term treatment, all hospitals concerned were asked to fill up a short questionnaire on the main features of the cases admitted. The first 391 cards returned have been analysed with the following result. They refer only to *confirmed* cases.

Table V shows the presenting signs and symptoms, the mental condition on admission and the result of the examination of the cerebrospinal fluid.

Table VI shows that 34.8% were abortive and 8.5% were cases of the bulbar type. From the point of view of preventive and social medicine the amount of residual paralysis is most important. Table VII shows that the case mortality was 5.1% and that 54.2% made a complete recovery. Table VIII divides the recovered cases according to the degree of severity of residual paralysis. There is a discrepancy with Table VII due to the fact that 11 of the 58 with "slight paralysis" were classed as "No (significant) paralysis" by the hospitals. In 28% of the genuine cases the attack was of the double-phase type giving a "dromedary" chart. In 6% of the total a respirator had to be used at some time or other. Overall, 25% of these 391 cases will probably have a limited working capacity and in 5% of the total this capacity will be almost nil. Table IX shows the distribution of the paralysis.

TABLE V.—HOSPITAL PATIENTS—PRESENTING SIGNS AND SYMPTOMS

Total Patients—391				
Symptom	No.	% of total patients		
Pyrexia	254	65.0		
Headache	265	67.8		
Vomiting	173	44.3		
Sore throat	75	19.2		
Stiff neck or back	257	65.7		
Constipation	51	13.0		
Abdominal pain	43	11.0		
Pains in limbs	181	46.3		
Paresis	101	25.8		
Paralysis	53	13.6		

Reflexes were diminished in 61.3 % of cases, normal in 33.0 % and exaggerated in 5.7 %.

<i>Mental Conditions on Admission</i>				<i>Examination of Cerebrospinal Fluid</i>			

TABLE IX.—PARALYSIS EXPERIENCED DURING COURSE OF ATTACK

Part of body affected	Bulbar type 33 cases				Spinal type 214 cases				Ascending type 8 cases				All types including 136 abortive cases. Total cases 391			
	Paresis		Paralysis		Paresis		Paralysis		Paresis		Paralysis		Paresis		Paralysis	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Cranial nerves	3	..	1	3.0	2	0.9	1	0.5	1	12.5	2	0.5	3	0.8	—	—
4	..	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
6	..	2	6.1	15.2	—	—	2	0.9	1	12.5	2	0.5	8	2.0	—	—
7	..	8	24.2	30.3	3	1.4	3	1.4	—	—	11	2.8	13	3.3	—	—
10	..	7	21.2	30.3	2	0.9	2	0.9	—	—	9	2.3	12	3.1	—	—
11	..	—	—	21.2	3	1.4	2	0.9	—	—	3	0.8	9	2.3	—	—
12	..	—	—	9.1	—	—	—	—	1	12.5	—	—	4	1.0	—	—
Diaphragm	..	—	10	30.3	5	2.3	7	3.3	5	62.5	5	1.3	22	5.6	—	—
Intercostals	..	—	12	36.4	25	11.7	29	13.6	5	62.5	25	6.4	46	11.8	—	—
Upper limbs, one	..	—	1	3.0	23	10.7	26	12.1	1	12.5	23	5.9	28	7.2	—	—
Upper limbs, both	..	—	9	27.3	9	4.2	20	9.3	6	75.0	9	2.3	35	9.0	—	—
Back muscles, one side..	..	—	—	—	5	2.3	2	0.9	1	12.5	5	1.3	3	0.8	—	—
Back muscles, both sides	..	1	3.0	6.1	15	7.0	37	17.3	1	12.5	16	4.1	40	10.2	—	—
Lumbar muscles, one side	..	—	—	—	5	2.3	1	0.5	—	—	5	1.3	1	0.3	—	—
Lumbar muscles, both sides	..	—	—	—	5	2.3	22	10.3	1	12.5	5	1.3	25	6.4	—	—
Abdominal muscles, one side	..	—	—	—	1	0.5	5	2.3	—	—	1	0.3	5	1.3	—	—
Abdominal muscles, both sides	..	—	—	—	9	4.2	28	13.1	4	50.0	9	2.3	34	8.7	—	—
Lower limbs, one	..	—	—	—	47	22.0	37	17.3	—	—	47	12.0	37	9.5	—	—
Lower limbs, both	..	—	6	18.2	25	11.7	55	25.7	6	75.0	25	6.4	67	17.1	—	—
Respirator	..	—	10	30.3	4	1.9	6	2.8	4	50.0	4	1.0	20	5.1	—	—
Nasal feeding	..	1	3.0	15.2	—	—	2	0.9	1	12.5	1	0.3	8	2.0	—	—
Intubation	..	—	—	3.0	—	—	—	—	—	—	—	—	1	0.3	—	—

* % of total cases in type group.

The normal procedure was to keep patients in the admitting hospital for about three weeks and then to transfer those needing special measures of rehabilitation to a long-stay suburban hospital where, in the case of children, education was available.

We may note here that the most common mistakes in diagnosis as revealed by an analysis of 71 unconfirmed cases out of 170 admissions to the Western Hospital under the care of Dr. Kelleher were as follows: Tonsillitis 10; rheumatism 5; cerebrospinal fever 3; lobar pneumonia 3; bronchitis 2; bronchopneumonia 1; tuberculous meningitis 2; cerebral tumour 1; cerebellar abscess 2; subarachnoid hæmorrhage 1; typhoid fever 1; measles 1; scarlet fever 1; chicken-pox 1; osteomyelitis 1; acute toxic polyneuritis 1; otitis media 1—a truly representative collection.

It has been a serious epidemic. Unfortunately, we have learnt little that is concrete about the epidemiology of the disease or its prevention, though certain trends observable elsewhere have been confirmed.

I must express to my colleagues, Dr. Scott, Dr. Breen and Mr. Benjamin, my very great indebtedness for help in compiling this paper and also the medical staff of a large number of hospitals, L.C.C. and voluntary, for the time and care they gave to filling up the questionnaire and finally I wish to thank the Medical Officers of Health of the City and the boroughs who have supplied much of the information as to local action which I have included.

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Some Atypical Primary Tuberculous Lesions

By MARGARET MACPHERSON, M.D.

BEFORE describing atypical primary tuberculous lesions, I will first give a brief account of the accepted views about typical primary lesions.

In many urban districts about 80 to 90% of adolescents of 15 years of age have been infected by the tubercle bacillus according to the results of tuberculin testing.

After comparison of this with the morbidity figures for tuberculosis, it is obvious that the great majority of primary lesions are innocuous. Most children become infected during the school age. Fortunately it is at this time of life that primary infections appear to have little effect on the children and healing of primary lesions usually takes place, but it is difficult to say just how complete that healing is. Is there left any unhealed portion which remains as a potential source of tuberculous disease in later life?

In young children and infants primary infection more often causes trouble than in school children. At this age, children may develop gross tuberculous lesions in the lung with large areas of tuberculous bronchopneumonia, or there may be generalized tuberculous lesions, spread through the blood-stream, with miliary tuberculosis with or without meningitis.

In others, changes secondary to the primary lesion may develop, changes which in themselves are not tuberculous, such as areas of collapse of lung resulting from occlusion of a bronchus due to enlarged caseating lymph nodes. If the infant does not succumb to the primary lesion, it is usual for these lesions to recover completely. The capacity which a child shows for healing and calcifying these lesions is often surprising. But again the completeness of the healing and the relation of these lesions to disease in adult life are matters which cannot yet be determined conclusively.

Over 14 years of age, the picture of primary infection differs once more. Although many of the primary infections at this age are harmless, some appear to have a direct association with the type of active pulmonary tuberculosis usually associated with adult life. Observation of young adults during the period of conversion of negative to positive tuberculin tests, and for some years afterwards, tends to support this suggestion. I would stress "some years after" because there may be a latent period when there is certainly very little in the way of clinical signs or symptoms, and even X-ray appearances may change very slowly.

Having dismissed the problem of primary infection in school children as being of less interest and importance than in other ages, I now propose to describe five cases of primary lesions, in school children, which did not behave in the usual way.

There is sometimes a tendency to adopt the attitude that, so far as tuberculosis in children is concerned, the disease is either fatal or else it is trivial in its manifestations and therefore the clinician need not be greatly concerned about it. My object in picking out these five cases is to illustrate that primary lesions in childhood may show interesting and unsuspected changes if the lesions are observed carefully over a period of years by X-ray pictures. The changes show that the lesions at times are unstable and therefore should not be ignored in spite of the fact that they produce no clinical symptoms or signs. Moreover, cases such as these may throw some light on the ætiology of adult pulmonary tuberculosis.

The last two cases show that primary lesions are not always circumscribed and can develop directly into infiltration typical of chronic pulmonary tuberculosis. The last case also shows how slow and insidious this process can be, a steadily increasing infiltration being without clinical manifestations for a period of years. The first three cases show that what appears to be healed lesion is not necessarily so, and that reactions around calcified lesions can occur and do so after the lesion has been calcified for a considerable time. They raise the questions: what is the relation between these reactions and active pulmonary tuberculosis? were these children fortunate in arresting the disease? might they, in adverse circumstances, have developed chronic pulmonary tuberculosis?

CASE I.—J. C., aged 4 years 8 months.

Contact.—Sister of 9 years with acute pulmonary tuberculosis and positive sputum.

History.—Recent bronchopneumonia but no symptoms now.

Clinical picture.—Normal healthy child. X-ray showed a primary complex with enlarged hilar shadow on left side and small indefinite shadow left mid-zone (fig. 1). The primary lesion healed in the usual way, leaving a small calcified lesion in left mid-zone and calcification at the left hilum (fig. 2). Five years after the original X-ray, routine X-ray showed reaction round the calcified lung lesion (fig. 3). No symptoms or abnormal signs. This reaction subsided within a few months but left a residual small oval shadow associated with the calcified focus, which was unchanged five years later. The boy is now 18 years, healthy and in the R.A.F.



FIG. 1



FIG. 2

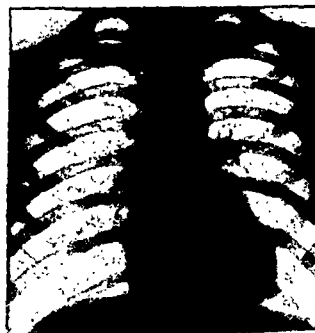


FIG. 3

CASE I: FIG. 1.—Primary complex with enlarged hilar shadow left side and indefinite shadow left mid-zone.

FIG. 2.—Calcified primary complex three years later.

FIG. 3.—Small reaction round calcified pulmonary lesion five years after first X-ray.

CASE II.—J. B., aged 4½ years.

Contact.—Mother and father died of pulmonary tuberculosis.

History.—No symptoms. Suffered from general debility from birth to 1 year old.

Clinical picture.—Normal healthy child. X-ray showed a large calcified lesion in right mid-zone, lateral view seen (fig. 4). Six months later said to have right-sided pneumonia, from which she recovered. Seen two months after this and X-ray showed reaction round the calcified lesion (fig. 5). Reaction subsided but at the same time calcified lesion decreased and disappeared. Fig. 6 shows lateral view, two years after the reaction developed, with no sign of previous calcification. Seven years later, at 14 years of age, X-ray is unchanged.

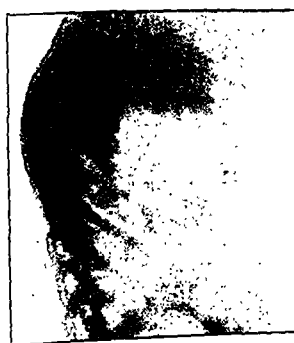


FIG. 4

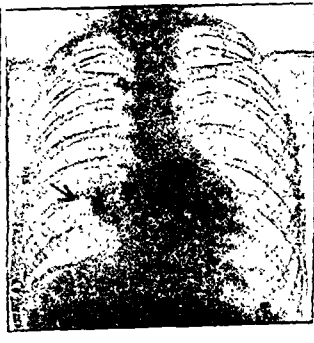


FIG. 5

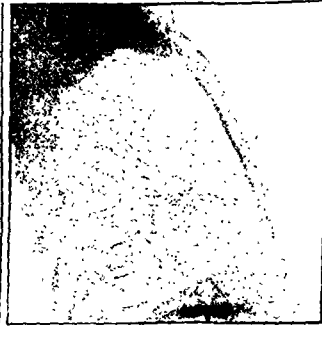


FIG. 6

CASE II: FIG. 4.—Lateral view to show calcified primary lesion.

FIG. 5.—Reaction round calcified lesion in right mid-zone, eight months later.

FIG. 6.—Lateral view two years after reaction developed, showing disappearance of calcified focus.

CASE III.—G. S., aged 10 years.

Contact.—Aunt slight.

History.—Recent anorexia, cough and pain right side of chest.

Clinical picture.—General condition poor. No abnormal signs. X-ray showed a large circumscribed opacity in the right upper zone with enlarged hilar shadow on right side, diagnosed primary complex. Healed in the usual way, leaving large calcified focus right upper zone and right hilum (fig. 7). Five years after the original lesion was found, when boy aged 15 years, area of reaction seen round calcified focus (fig. 8). No symptoms or signs at this time or subsequently. Opacity cleared after a few weeks, but calcified lesion much smaller and decreased considerably in size. X-ray at age of 23 years shown (fig. 9).



FIG. 7



FIG. 8



FIG. 9

CASE III: FIG. 7.—Calcified primary complex right lung.

FIG. 8.—Two years later, reaction in second and third spaces, round calcified focus.

FIG. 9.—Reaction subsided and area of calcification decreased.

The next two cases show atypical reactions to the initial infection.

CASE IV.—A. R., aged 10 years.

Contact.—Lodger, ill recently with pulmonary tuberculosis.

History.—Recent pyrexial attack of unexplained cause. Well when first seen.

Clinical picture.—Healthy child. No abnormal signs. X-ray showed left hilar shadow enlarged, and flocculent shadow left upper zone (fig. 10). After initial increase in shadow (fig. 11) it slowly decreased, becoming localized to small lesion one year later (fig. 12), subsequently showing only a small calcified focus in left upper zone and in left hilum. Girl now 21 years, in good health and X-ray unchanged for five years.

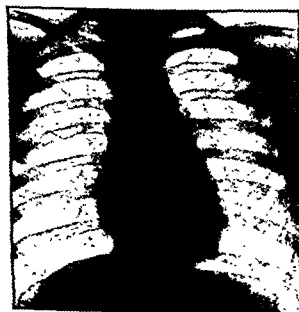


FIG. 10

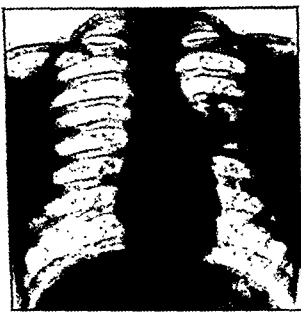


FIG. 11

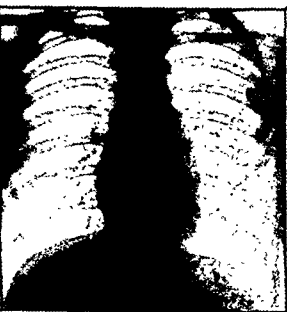


FIG. 12

CASE IV: FIG. 10.—Primary complex with enlarged left hilar shadow and diffuse lesion left second and third spaces.

FIG. 11.—Four weeks later. Increased flocculent shadow left lung.

FIG. 12.—One year later, calcified lesion left hilum and small localized lesion left second space.

CASE V.—S. G., aged 12 years.

Contact.—None.

History.—Recent cough. Attended hospital. No abnormal clinical or X-ray signs. Mantoux O.T. 1/100 negative. Was asked to attend two years later so that Mantoux test might be repeated for research purposes. Found to have Mantoux 1 : 10,000 positive and X-ray showed flocculent shadow right upper zone (fig. 13). Has been kept under supervision for seventeen years. During first nine years has shown slow progression of disease through right upper lobe and spread to left apex, and at same time healing of early lesions (fig. 14). First symptom was slight transient hæmoptysis five years after first positive X-ray (fig. 15). Fig. 16 shows further healing of right apex but spread to left side. Nine months later she had pain right side, fever and lassitude, and X-ray showed cavity at right apex (fig. 17). After sanatorium treatment cavity disappeared and there was retrogression of the lesion from that time. Fig. 18 shows state of lung five years later. From this time there has been little change and the girl is well and due to be delivered of her second child in three months' time.



FIG. 13



FIG. 14



FIG. 15

CASE V: FIG. 13.—Primary lesion with flocculent shadow right second space.

FIG. 14.—Three years later, shows diminution of original lesion but increased infiltration above.

FIG. 15.—Five years later, increased lesion right apex.

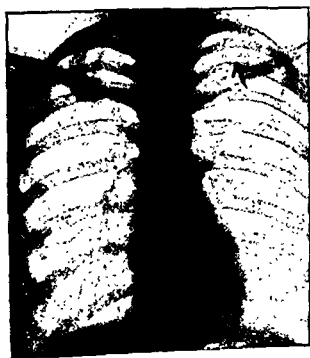


FIG. 16



FIG. 17



FIG. 18

CASE V: FIG. 16.—Seven years later, right apical lesion less but infiltration seen left apex.

FIG. 17.—Seven years and nine months later, cavity at right apex.

FIG. 18.—Twelve years later (aged 26). Lesions decreased and now stationary.

Section of Ophthalmology

President—HAROLD LEVY, F.R.C.S.

[October 9, 1947]

Leucosarcoma of Iris (Unpigmented Malignant Melanoma).—T. H. WHITTINGTON, M.D.

Married woman aged 64.

No history of past injury, or of inflammation, or of recent illness. Present history: one attack of acute pain in left eye on September 15, 1946.

On examination four days later a hæmorrhagic yellowish, lobed nodule was seen protruding from anterior surface of iris. Small hyphæma and blood clot which appeared to have come from the tumour cleared in five days. Vision 6/9.

Investigations.—On examination, nothing abnormal was found.

Diagnosis.—The growth in the eye does not appear to be cystic, and does not transilluminate; it does not appear to be tubercular or syphilitic, and there is an almost total absence of inflammatory reaction. It might be an encysted foreign body with fibrosis around but there is no history or sign of penetration. It is probably a new growth. Isolated new growths of the iris, i.e. not associated with growths of the ciliary body or elsewhere in the eye, are rare. Martin-Jones (1946) mentions only 4 cases of isolated sarcoma of the iris out of 263 cases of uveal sarcomata; one of these 4 had a spontaneous hyphæma, but all 4 were clinically pigmented. A clinically unpigmented growth is very rare. Duke-Elder and Stallard (1930) described a case and were able to collect only 25 other cases from the literature. Spontaneous hyphæma is also rare. Wood and Pusey (1902), in a review of 64 cases of sarcoma of the iris, state "an interesting symptom, which has been observed in these cases is recurrent hæmorrhage into the anterior chamber. Such bleedings tend to occur spontaneously, and have several times been the cause of sending patients to the doctor".

Treatment.—Operation on October 12. A corneo-scleral stitch—as used in cataract extractions—was put in at the margin of the cornea and a large conjunctival flap turned back; a scratch-through incision was made with a Graefe knife, extending from 1 o'clock to 5 o'clock. Then the corneal side of the wound with the stitch was lifted up and a very large basal iridectomy from 1 o'clock to 5 o'clock was made. After roughening the corneal epithelium at the edge, the conjunctival flap was slipped over the wound.

Histology (Dr. L. Woodhouse Price).—"Malignant melanoma. Morphologically the component cells are of spindle form and arranged in whorls. Intracellular pigment is fairly copious and is seen both in the tumour cells and in histiocytes or chromatophores. In the former, the pigment granules are of delicate form and of golden-brown colour. In the latter, on the other hand, the pigment assumes the form of coarse granules of dark-brown or black appearance. The presence of iron pigment was excluded by the application of the Prussian blue staining reaction. Moreover, the presence of the melanin was proved by intensification of blackness by ammoniacal silver solution. Ontogenetically this tumour arose from a nerve end organ. Enucleation of the eye is indicated."

On December 3, 1946, patient had quiet eye, vision 6/9. In view of the spindle-celled character of the tumour with scanty mitoses, and the fact that it seems to have been removed completely, and that iridectomy has been reported as successful in similar cases, the eye has not been removed.

REFERENCES

- DUKE-ELDER, S., and STALLARD, H. B. (1930) *Brit. J. Ophthalm.*, **14**, 158.
 MARTIN-JONES, J. D. (1946) Uveal Sarcomata, *Brit. J. Ophthalm.*, Monograph Suppl., **11**.
 WOOD, C. A., and PUSEY, B. (1902) *Arch. Ophthalm.*, **31**, 323.

Mr. Williamson-Noble suggested one point in treatment, namely, to have some human thrombin put in the anterior chamber first. This might prove very helpful.

Mr. H. B. Stallard said that malignant melanoma of the iris showed no histological evidence of karyokinesis and so were relatively slowly growing. They are radio-resistant. The prognosis is good after removal of the growth with the adjacent iris. Excision of the eye for a nodular malignant melanoma of the iris not infiltrating the filtration angle nor touching the cornea was quite unjustifiable.

He described the case of a girl, aged 16, who had a malignant melanoma of the iris in 1931 and was treated unsuccessfully by unscreened radium. The neoplasm was removed by iridectomy. Histological examination showed no evidence of effective irradiation. The patient is still alive and well sixteen years after operation and has shown no signs of recurrence nor of metastases.

Melanosis of Conjunctiva.—A. S. PHILPS, F.R.C.S.

Mr. Philps said that this was a case of a lady aged 45, who for the past five years had had an increasing melanosis of the conjunctiva of the left eye (figs. 1 and 2). Lately the pigment had invaded the cornea as well though none appeared intra-ocularly. Vision in this eye was 6/6. A piece of conjunctiva had been excised and sections of it were shown.

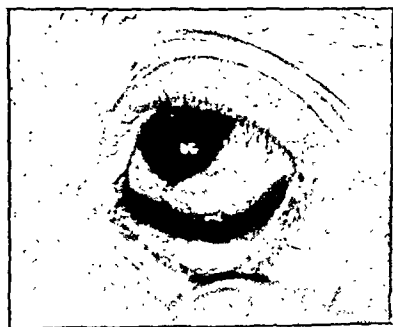


FIG. 1

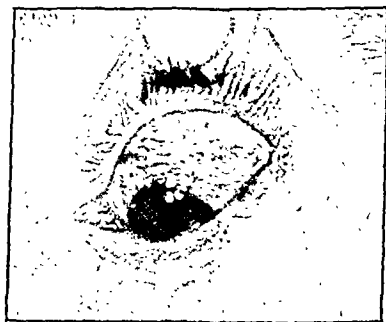


FIG. 2

FIGS. 1 and 2.—Melanosis of the conjunctiva present for five years and increasing slowly. The patient uses no eye drops of any kind.

Mr. Eugene Wolff said that the point of interest was that the section showed an ordinary nevus—a mass of nevus cells almost without any cytoplasm—and around this downgrowths of pigmented epithelial cells. This was very unusual in melanosis. Some sections showed the cells proliferating and revealing early malignant changes.

Mr. G. T. W. Cashell said that he had described to the Section in 1940 (*Proc. R. Soc. Med.*, **33**, 545) a case of an old lady aged 70. He had excised a small tumour of the limbus; on section it showed malignant melanoma and he had exenterated the orbit.

This condition was described by Reese (*Arch. Ophthalm.*, 1938, **19**, 354) when he mentioned 8 cases of what he called precancerous melanosis of the conjunctiva. Reese had suggested that these cases should be watched very carefully. The onset of malignant change was usually accompanied by a severe inflammatory reaction in the eye, and that was the time to exenterate the orbit.

The President said that it had struck him that this pigment was distributed all over the local area, but there was no sign, as far as he could see, of any growth. Of course, if it was found that there were malignant cells, this made the treatment more obvious than it would otherwise be.

Hereditary Hæmorrhagic Telangiectasia with Conjunctival Lesions.—Major HOWARD REED, R.A.M.C.

This patient, aged 19, complained of excessive blinking, a feeling of "something in the eyes", and he had frequent epistaxes. His mother, when she was alive, suffered from frequent nose-bleeds, and a younger brother has had several epistaxes. Telangiectases were present on the palpebral conjunctivæ, nasal mucosa, tongue, buccal mucosa, and skin (figs. 1 and 2). No miliary aneurysms or other lesions could be seen in the fundi and the blood-count was normal.

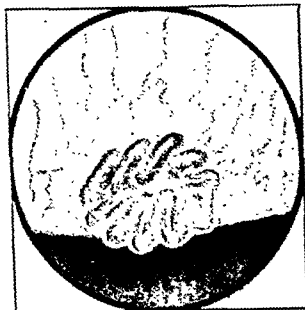


FIG. 1

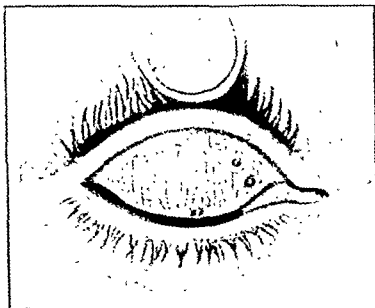


FIG. 2

ALEXANDER

Everted upper lid of right eye to show conjunctival lesions in case of hereditary hæmorrhagic telangiectasia. FIG. 1.—Slit-lamp appearance of telangiectasis. FIG. 2.—Macroscopic appearance of telangiectases.

The salient features of the disease were described by Osler as hereditary hæmorrhagic telangiectasia, with several family trees which showed a dominant inheritance with equal sex distribution. The condition usually becomes apparent soon after adolescence by recurrent attacks of bleeding from the nose. Hæmatemesis, hæmoptysis, hæmaturia, and even cerebral hæmorrhage have been described in association with this condition.

Appreciation of Form and Colour after Cataract Operation.

Mr. F. A. WILLIAMSON-NOBLE exhibited two landscape paintings executed by a patient, one before and the other after operation for cataract. He said that various differences were perceptible between the two renderings, especially in the colouring and detail of the skies. The clouds, for example, were seen much more clearly after the operation. What was most remarkable was the difference in the size of objects. The post-operative landscape was definitely smaller in scale than the pre-operative one, and that tallied with experience of other patients after cataract operation—the 6/6 line was equivalent in size to about the 6/9 line in the case of someone who had not undergone the operation.

Stereoscopic Pictures.—Mr. F. A. WILLIAMSON-NOBLE also showed a new method of stereoscopic photography which, he said, was likely to be of value in ophthalmic work. He had been loaned ten pictures by the Austin Motors Corporation, who had been using the method. Two devices are used—one for photographing small subjects at not more than 10 ft. (3.05 m.) distance—is a camera which travels in an arc and 24 pictures are taken in ten seconds. For larger pictures a 24-lens camera is used, the lenses being disposed in two horizontal lines each of twelve. The combined print is covered with a fine optical grid which ensured a selective view by the two eyes.

Considerations on the Treatment of Detachment of the Retina¹

By Professor H. ARRUGA (Barcelona)

AFTER Gonin's publication of the results obtained by his operation for detachment of the retina, those of us who practised this operation at the time were successful only in about 25% of cases. The perfecting of technique has caused this percentage to rise to as much as 70 or 80, taking into account all operated cases indiscriminately. This percentage of cures, attained in the last six or eight years, cannot easily be exceeded in spite of our increased experience.

Of the 20% or 30% of patients on whom we operate but cannot cure, we know beforehand that about half are unlikely to be successful, either because of the difficulties they present (very large or multiple rents, opacities in the media, subjects with systemic disease, &c.) or because of the age of the lesion; but, in the other half of that 20% or 30% of uncured cases, we had hoped to effect cures because we had succeeded in other similar cases, and our failure is due to abnormal developments in the curative process.

In my experience there is no type of detachment in which 100% of cures is obtained. The only cases in which I have obtained cures without complications are those in which I have diathermized rents without detachment or with a hardly perceptible detachment, that is, cases in which the retina had not yet detached, and the edges of the rent did not show any appreciable unevenness when examined through the ophthalmoscope. In such cases even a slight diathermic application is observed at once by ophthalmoscopic examination owing to the coagulation of the retina. In these cases the early symptoms of floating opacities or hæmorrhages into the vitreous led the patients to consult an oculist and so facilitated the discovery of a recent rent, the rupture of whose vessels provoked the hæmorrhage in question. In most of these cases there had already been a detachment of the retina in the other eye (and the patient's sharpened observation of these symptoms has made early treatment of the retinal rent possible). I have operated on 23 cases of this type of recent rent without detachment with perfect results and without any loss of visual acuity; of course, in none of them was the perforation situated at the macula. I have also invariably had perfect results in diathermizing areas of intense vacuolar degeneration of the retina without detachment. This type of retinal degeneration is frequent in the supero-external area parallel to the equator, and in cases where there has already been a detachment of the retina in one eye, diathermy of the degenerated area in the other eye can legitimately be practised. As an extra precaution in such cases, I have used a low current, just enough to coagulate the retina slightly. I start with a very weak current and increase its intensity until the coagulation of the retina is obtained. The intensity of the current varies in each case, but sometimes currents of as little as 10 to 15 milliamperes are effective.

Detachments of a favourable anatomicopathological type which run an unfavourable course.—Apart from the cases in which there is only slight or no detachment of the retina, there is always a possibility of complications, even in the simplest cases. For instance, I have had occasion to operate on cases in which detachment was reduced by bandaging and rest for six days, at the end of which it had almost disappeared. In these conditions, I operated on the patient with surface diathermy, and at the end I was convinced that he would get cured, yet the development of the disease was unfavourable. The patient developed slight pains and photopsiæ. In spite of further rest and the institution of treatment including penicillin, on the remote chance of there being some infection, the condition of the eye did not improve. The area around the rent appeared turbid and the detachment spread in all directions.

¹Dr. Arruga illustrated his talk to the Section with numerous pictures.

The only explanation I can offer is that the choroid was in a peculiarly sensitive condition, owing to the existence of a chronic inflammatory process, so that the action of the diathermy was intensified.

I cannot see how such an unfavourable development could be foreseen in a case which was apparently so easy to cure. Only when a patient presents a local reaction or has any pain, or when the vitreous is turbid round the rent, without the turbidity being due to blood, can we suspect that the choroid is inflamed or likely to become excessively inflamed by diathermy.

This excessive reaction is observed more frequently in certain patients who have been operated on previously; and this led Weve to think that such cases were anaphylactic. I believe the irritability of the choroid is due to the fact that it has been inflamed previously, and that this inflammation had not disappeared at the time of the second intervention.

Detachment starting at the macula.—In a detachment at the macula, the rent is very small and is very difficult to cure. Although this is the type of rent whose start is soonest noticed by the patient since it affects central vision, the rest cure does not improve it as it does most detachments with small rents when the patient is made to rest in bed with the eyes bandaged.

These rents at the macula are not increased by movement, as are all other types, probably because macular rents are not caused by traction of the vitreous on the retina by means of adhesions between its framework and this membrane, but by choroidal exudation which pushes the retina towards the centre of the eyeball and tears it circularly near the centre of the macula, where it is very thin.

The retina in the macular area is more adherent to the choroid than elsewhere except at the ora serrata where adhesion is even firmer. It is due to this mechanism of the formation of macular rents that they are round and have no floating shred such as round rents have in other retinal areas; here the shred remains adhered to the choroid.

The fact that sometimes the macular rent is secondary, for example, that it may occur when a detachment initiated by one or more rents in another area reaches the macular area, confirms this mechanical process, its production by the retina being pushed into the cavity of the eye by subretinal fluid.

The pathogenesis of detachments of the retina starting with macular rents raises a therapeutic problem necessitating care in applying diathermy (as is indeed always necessary in view of the functional importance of this area); moreover, the subretinal fluid should be drained through a sclero-choroidal puncture at some distance from the central area and in the lower part of the globe, where the detachment is usually greatest.

Detachment of the ora serrata.—One of the features of this kind of detachment is the small influence of rest. The retina never becomes reattached in its original position, even as a result of a successful operation. Success can only consist in getting the retina joined to the choroid throughout the sector which borders the retinal aperture.

As a result of this condition the retina does not become adapted to the choroid by rest, even when punctures are made during the operation to drain off the subretinal fluid at the level of the disinsertion. In these punctures we do not obtain a fluid which is progressively yellower with the age of the detachment, as occurs in the other types of detachment; what we get is a liquid of a viscosity similar to that of the vitreous.

The reason why the retina cannot be adapted to the choroid in cases of disinsertion at the ora serrata is probably that the retina is affected with an inflammatory or degenerative process, either of which is followed in its natural development by atrophy and retraction of the retinal tissue proper.

As a consequence of this the retina must be diathermized at the point where it still touches the choroid, or is very close to it. We have to try to verify with the ophthalmoscope whether the retina is coagulated with a characteristic whitish colour if we are to expect a cure, and this is often not obtained unless we diathermize near the posterior pole; but we have to sacrifice some peripheral visual field in order to preserve the central visual field and cure the disease by strictly limiting the detached area.

It is useless, and often harmful, to diathermize the retina in the peripheral part where reattachment is not possible.

The following case was unusual both by its gravity and by the fortunate cure already described in my first book on detachment of the retina.

This was a patient who was blind in the right eye owing to an old detachment and whose left eye showed a detachment. In an attempt to improve the local condition by rest, she was put to bed with a binocular bandage. After a month there was no improvement. The patient was operated on by diathermy applied over the entire vertical meridian, passing behind the optic nerve on its internal part. Fortunately, the detachment was restricted thereby and, at the end of a year, the patient had 0.2 vision in that eye.

It is curious to note that the choroid, which still had the characteristic red colour at the end of a year, five years later—that is, six years after the start of the disease—was totally atrophied, and the detached retina was almost transparent and bloodless, its vessels having almost disappeared.

This atrophy of the choroid is verified histologically in all the microscopic preparations of enucleated eyes where there had been an old detachment of the retina, a fact which proves that the vitreous is not tolerated by the choroid. This explains why, in some detachments, this intolerance of the choroid to the vitreous asserts itself by uveal reaction (turbid vitreous, a poorly reacting pupil, ciliary injection), which is certainly unfavourable for the progress of the disease.

Inferior detachment.—This kind of detachment also has an anomalous development owing chiefly to the fact that it may go on for some time without being noticed by the patient. This development is due to the subretinal fluid occupying the inferior region of the eyeball, where, owing to natural development and to its weight being greater than that of the vitreous, the fluid is displaced in all cases of detachment; this makes the progress of detachment slower when it starts in the lower part of the globe.

On the other hand, the reduction of the field of vision caused by the detached area of the retina is not readily noticed by the patient, because it occurs in the upper part which is already much reduced by the superciliary arch; indeed it is not clearly perceived until it reaches 55° or 60° in the vertical meridian, corresponding to about 14 mm. distance from the corneal limbus, a little behind the equator.

Consequently when we see a detachment of the retina restricted to the lower part, either with a disinsertion or with rents near the inferior pole, it is difficult to know when exactly it started. Patients can help us if they have noticed photopsiæ or floating opacities in the vitreous; but we frequently can form no accurate estimate of the age of the lesion. Sometimes the patient has noticed it only for a few days, and on examining him with the ophthalmoscope we see unmistakable signs that the detachment is old: for instance, folds in the retina and pigmented lines, which lead us to infer that the lesion is months, or even years, old.

If the detachment is recent, diathermy of the torn areas is the best technique; but if it is old, this is useless, since a choroid that has been in contact with the vitreous for some time cannot possibly react. In such cases, we must be content with limiting the area of detachment by means of a barrier of retino-choroid adhesions, similar to that which is made in cases of disinsertion in the ora serrata.

In some of these cases, the detached portion, although well-defined and limited, produces symptoms which are a continual source of alarm to sensitive patients. These may be photopsiæ, and floating opacities (*muscæ volitantes*), which are inevitable if any part of the retina is detached and moves with the movements of the eyeball. If the patients are good observers, they realize that the photopsiæ are confined to the area of the detachment whereas the floating opacities extend beyond it. If the photopsiæ go beyond the detached area, we must examine the field of vision to verify whether the detachment is spreading; this can also be seen by ophthalmoscopic examination as a slight opalescence of the retina, similar to that found in œdema of the retina. If there is such spreading of the detachment, we must apply diathermy slightly in the affected area.

Sometimes the well-defined area of the retina shows an accentuated bulge which remains the same for many years. At first such cases worried me a great deal as I feared relapses, but fortunately when the union between the choroid and the retina is firm, they do not relapse.

And thus I end this *exposé* of these aspects of the treatment of detachment of the retina. The subject is indeed a complicated one, owing to the great diversity of clinical types and, consequently, of techniques to be followed.

In conclusion, I cannot fail to pay tribute to our master Gonin to whom we owe it that one of the diseases in ophthalmology which was always thought to be incurable can now be cured in most cases.

Sir Stewart Duke-Elder congratulated Professor Arruga warmly on his lecture, saying that there was no one in the world who spoke with greater authority on this subject. The fact that 70% or 80% of successes had been recorded in a series of cases of this type was due to no one alive more than to Professor Arruga himself. There were one or two things which were (to the speaker) extraordinarily interesting. For example, there were the cases in which the retina showed a small hole readily accessible and presenting every appearance favourable for treatment, but which nevertheless did not do well at all. He himself had had a case of this type about two months ago. He thought at the time that the unfavourable result of the operation might have been due to excessive reaction. The case showed a small hæmorrhage in the retina some distance away from the hole, but the only result of operation was to convert the single hæmorrhage into several and a partial detachment into a total one. Such a result was quite possibly due to the exacerbation of a pre-existing pathological condition of the choroid making it react in an unusual way to diathermy. Another point of interest was Professor Arruga's technique of the adaptation of the procedure at operation to the age of the lesion, diathermy over the torn areas being practised if the detachment was recent, whereas if it was old, the best procedure was to diathermize round about it to limit the area of detachment by means of a barrier of retino-choroidal adhesions.

The author had given them not only an exposition of the general subject, but had added those personal touches from his own practice which only an expert of great experience could give. He wished to comment in particular upon the excellence of his illustrations. Professor Arruga made all his drawings himself by a technique which he had worked out, not painting them in the usual way but by using a spray and stippling. The results were excellent and added greatly to the value of his exposition.

Mr. Humphrey Neame said that he desired to bring to Dr. Arruga's notice an illustration of a retractor modelled on his own retractor but made of a plastic material for carrying and projecting the light. Some of the reflected light reached the terminal part of this material and this was distributed over the surface of the eye. His instrument, which had been made about four years ago, illuminated the area very well in addition to its giving one a view down the tunnel of the speculum. This had been reproduced in the *British Journal of Ophthalmology* (1943), 27, 310. A new modification was a 6-volt bulb, which was considerably better than the bulb of weaker intensity previously used. In dealing with the upper or lower parts of the field it was better to remove the eyelid speculum and view with this instrument alone.

Mr. A. S. Philips said that to find that the detachment had increased after operation was probably something that had happened to all of them. He personally would have thought it due to a thrombosis in the major branch of one of the vortex veins, or perhaps the vortex vein itself. If such a thing happened it might be that the back pressure caused exudation and the separation of the retina to a greater extent than before operation. He had explained this by saying that where it so happened it was because of too much reaction which had brought about thrombosis in the choroidal vein or perhaps the main trunk of the vortex vein itself.

Mr. G. W. Black said that he had been most impressed by the boldness shown by Dr. Arruga in tackling holes with no associated complications and in the treatment by diathermy of areas of retinal degeneration, thought liable to be the starting point of detachment. Did Dr. Arruga never hold his hand? He recalled his own experience that roughly 7% of cases spontaneously recovered following a period of rest without recurrence of the detachment and that such cases might show tears in the beginning or might not. In some bilateral cases, one eye might recover and never need surgical treatment, whereas the other required operation. Did the author not think that the presence of a detachment in some cases caused a mildly irritant reaction which offered some possibility of natural cure?

Dr. Arruga, in reply, spoke of the importance of dealing with tension as part of the cure. If he had a large separation and the patient showed no signs of getting better with rest he would carry out a puncture in the sclera and choroid, but in his experience this had not been very satisfactory, and in fact he had had a number of bad results with puncture before operation. As for detachment in the aphakic eye, he said humorously that he would be able to answer that question in thirty years' time. He had experienced more detachment with intracapsular than with extracapsular extraction—he did not know why. He could affirm that detachment was not the consequence of operation, but the consequence of the lesion in the retina.

Dr. Arruga found some difficulty in making himself understood in English, and spoke in French and was interpreted by the President (Mr. Levy) from this point. He said that in all detachments they knew that there were two processes by which this could be caused: (1) retraction of the vitreous and (2) the pushing forward of the retina by the choroid, the retina itself remaining passive. In any given case it was not known exactly which of these two processes might be operating. In detachment the curative organ was the choroid. This was the vascular organ of the eye and could absorb the subretinal fluid. Therefore if there was any atrophy of the choroid absorption was not possible and a cure could not be obtained. The exudative power of the choroid was also important because upon this depended the formation of adhesions between the retina and the choroid. Therefore it was important that neither the absorptive nor the exudative power of the choroid should be destroyed, and treatment must be directed as far as possible to avert such destruction. The operative interference must be sufficient to produce exudate and to seal down the detached retina at the same time leaving sufficient undamaged choroid to absorb the subretinal fluid. Unfortunately the state of the choroid before operation was not known. It was to be hoped that an investigation of this problem might be carried out in the future.

As a result of observations made some years ago it was known that the retina did not detach (except as the result of accident) unless diseased and that the actions of the retina and choroid were interdependent.

The President thanked Dr. Arruga in the name of the Section for his interesting paper.

Section of Urology

President—WALTER W. GALBRAITH, M.B., F.R.F.P.S.

[October 23, 1947]

Modern Trends in Prostatic Surgery. [Abridged]

PRESIDENT'S ADDRESS

By WALTER W. GALBRAITH, M.B., F.R.F.P.S.

SIR PETER FREYER was the first President of this Section of the Royal Society of Medicine (1920) and it is to him more than to anyone that we owe the earliest successful form of treatment for prostatic obstruction.

Freyer's operation held the field in Britain for twenty-five years. It was the operation of choice for the general surgeon but few achieved results comparable with those reported by Freyer (1901-09-11). Haemorrhage and sepsis, at and following operation, and later obstruction, were common and generally the mortality rate was high.

In an endeavour to improve on the Freyer operation Thomson-Walker (1920) introduced an operation whereby an effort was made to control the bleeding at the operation, to lessen sepsis and to prevent post-operative recurrence of obstruction. Although in skilled hands it resulted in a diminished mortality and a greater freedom from complications this operation proved too complex for the average general surgeon, who continued to use the much simpler Freyer method.

About 1930 the treatment of prostatic obstruction was still unsatisfactory and the mortality in general hospitals was estimated to be about 20% although in special hospitals, such as St. Peter's, it was reported as 9.9% over a twenty-nine-year period but fluctuated in different years from under 5% to 14.5% (Thomson-Walker, 1936). From that time all our efforts have been directed to improving pre-operative, operative and post-operative methods in the hope that the incidence of mortality and morbidity might be lessened not only in a few special clinics but generally throughout the country. We are still, however, seeking a method which is simple, safe and sound. Some success has been achieved and to-day results generally show a definite improvement on those of twenty years ago. There is still, however, considerable divergence of opinion regarding the selection of operative procedure in the treatment of prostatic obstruction. Urologists should be thoroughly familiar with the various techniques: they can then adopt the method which they consider most suited to the patient, to their own skill, and to the particular circumstances.

I will now review the methods of treatment in vogue to-day and the conclusions concerning them at which I have arrived as a result of twenty-five years of urological practice.

(1) *The Freyer operation.*—This remains the most commonly practised method of prostatectomy among general surgeons, who frequently refer to the good results they have achieved with it. Whilst this may be so on occasion, on the average the post-operative discomfort, the long convalescence and the end-result surely indicate the undesirability of such a technique except where the poor physical condition of the patient necessitates a very short operation. Where a thirty- or forty-minute operation cannot be contemplated and in certain other cases governed by special factors, the Freyer operation, or rather its present modification, is of value. By "modification" I mean a moderate-sized incision, a quick and clean enucleation of the gland, adequate control of bleeding by a suitably sized Foley indwelling urethral catheter and closure of the bladder wall around a small or medium-sized Freyer drainage tube. This tube should be removed whenever the possibility of clotting is over, say in twenty-four hours, and after a further twenty-four hours the Foley catheter should be replaced by an indwelling No. 22 F size urethral catheter. These measures generally obviate the use of the suprapubic box. The wound heals rapidly, fistula formation is less likely or of short duration, and removal of the catheter on the tenth day generally ushers in natural micturition. I have found this the operation of choice in approximately 10% of my cases.

(2) *The Thomson-Walker operation.*—This improvement on the Freyer operation was first popularized by the late Sir John Thomson-Walker (1920, 1936). Since the advent of the closure operations I have ceased to use the Thomson-Walker operation and I see no useful place for it to-day.

(3) *Per-urethral resection*.—This method, in its present form, originated in America about 1930 and soon was acclaimed as the ideal treatment for all forms of prostatic hyperplasia. Not only were members of the medical profession swept off their feet by a wave of enthusiasm but the general public, having heard of the new method which obviated a "cutting operation", demanded it. Few now make use of it for every prostatic hypertrophy; most reserve it for the treatment of fibrous glands, the small subcervical adenomata and the case of obstructing carcinoma with impending or actual retention. In America the Mayo Clinic use it in preference to any other form of treatment and Emmett (1944) reports that for the ten-year period preceding 1942, 9,000 resections were performed there with a mortality rate of 1.1% and an average hospital stay of 8.6 days, only 3% requiring further resection at a later period for recurrence of obstruction. In England, Wardill (1947) also uses this method exclusively. He states that his cases are entirely unselected and that he has performed 537 resections during the twenty months prior to August 1947. 26 patients died (4.84%) and 58 required more than one resection (10.8%). On the other hand Millin (1946) after performing 219 resections discarded it, on account of late complications, except in the type of case I have specified. Chapman (1947) states that till recently he employed the method exclusively except for certain bad risk cases which were treated by permanent suprapubic drainage. He reports 379 cases with 24 deaths (6.3%). His present practice is to treat the large adenomatous prostate by suprapubic prostatectomy and 20% of his patients are now so treated.

There are two different methods of performing this operation: (1) by the McCarthy instrument using a cutting loop activated by diathermy electric current to excise the tissue, and (2) by the cold punch instrument, known as the Thompson resectoscope or punch, by which tissue is removed by a circular knife. The McCarthy instrument was first in the field and I gave it an extensive trial. Although of large size the shaft of the instrument required little movement in the urethra during the operation and thus I found the incidence of post-operative stricture was less than when using the punch instrument; its disadvantages were that the lens system, becoming clouded by blood, reduced visibility and made it difficult not only to recognize anatomical landmarks but to resect sufficient tissue and furthermore the operation tended to be prolonged as after each cut the telescope and cutting loop had to be withdrawn with the attached piece of tissue. I discarded the method when I acquired a Thompson punch which I found much simpler to use in that it permitted good visualization despite appreciable hæmorrhage and thus one was able to remove a large amount of tissue in a comparatively short time.

I have performed per-urethral resection on 26% of my cases and that includes a period of one year during which, to gain experience, I used the method almost exclusively: the results are shown in Table I.

TABLE I

Type of patient	Number	Died	Mortality percentage
Private..	69	7	10.14
Hospital	86	8	9.3
Total	155	15	9.6

My reaction to the operation, using the cold punch, is that I dislike the large size of the instrument which is stated to be size 30 F but which actually is often size 32 F and thus too large for the normal urethra. A smaller instrument is made but it is much less effective and seldom used. Many of my cases developed severe urethral stricture as a result of the passage of the large instrument. How could it be otherwise when one considers the tightly fitting instrument in the urethra with its constant piston-like movement against the delicate urethral mucosa? It is true that stricture formation can be partially obviated by inserting the instrument through a urethrotomy opening in the bulb but most of us would hesitate to perform this additional, even temporary, mutilation. A further difficulty I found with the instrument was in determining when a sufficiency of tissue had been resected. Time and again I considered that I had removed all obstructing tissue only to find a few days later that the patient still had difficulty in micturating freely or even that retention was still present. A further resection was then carried out and indeed at times resection was necessary on three separate occasions. I believe that this is not an uncommon occurrence but I am willing to admit to some inexperience. Presuming a man to be an ordinary skilled instrumentalist how many resections should be necessary before he could expect to achieve reasonable perfection? I have heard various estimates of from one hundred to three hundred but that seems an immensity of suffering to inflict in the pursuit of even a moderate degree of skill by this method! But there are other defects and the most important of these are hæmorrhage and sepsis. The operation cannot be performed without very considerable blood loss which starts with the first cut and is continued for several hours following it. The blood loss can be made good by transfusion although that is only necessary in a few cases but to prevent

clot retention the bladder must be washed out at short and regular but increasing intervals for some hours following operation. To my mind this is one of its most unattractive features as instead of the patient being permitted to rest quietly and sleep in his bed during post-operative hours, he is continually disturbed by the rapid filling and emptying of the bladder every few minutes. Furthermore in the odd case a return to theatre for re-examination and coagulation of bleeding points may be required. The application of a solution of "thrombin topical" to the bleeding surface may lessen or remove this sequel to the operation and early reports on its use for this purpose are encouraging.

Sepsis is another and not uncommon complication following this type of operation but the introduction of the sulphonamides and penicillin has undoubtedly lessened its incidence. Recurrence of the obstruction is an acknowledged possibility which may occur at a later period in an appreciable number of cases and a permanent incontinence though rare in the hands of the expert may be a serious complication to those less skilled. Thus I have concluded that, at least so far as I am concerned, per-urethral prostatectomy in the presence of a large adenomatous gland is a much more serious procedure than the radical suprapubic operation and that the results are less satisfactory. I now confine the use of this operation to the types of obstruction to which I have already referred.

(4) *The Harris operation* (1927, 1929, 1933).—My experience with this operation is shown in Table II.

		TABLE II	
Type of patient	Number	Died	Mortality percentage
Private	188	8	4.2
		(2 cardiac failure, 1 uræmia, 1 recurrence of cerebral thrombosis, 2 mesenteric thrombosis, 1 cerebral hæmorrhage one month later, 1 retroperitoneal infection)	
Hospital	130	4	3
		(1 phthisis two months later*, 2 excision of bladder tumour + prostatectomy, 1 uræmia six weeks after leaving hospital*)	
Total	318	12	3.7

*These two cases are, strictly speaking, not operation deaths. If they are excluded the hospital mortality is reduced to 1.5% and the total mortality to 3.1%.

The few modifications I have made in the original technique are I think of importance and have contributed to the results achieved. They are that the anterior transverse suture is passed widely, deeply, and tangentially to the cavity which the needle should not perforate; it should just miss its front wall. I think this stitch is a great factor in controlling hæmorrhage. The second transverse suture transects the cavity and should also be passed widely and deeply and parallel to the first suture but ample room must be left for the indwelling catheter which must not be gripped tightly and in fact the reconstructed internal urethral meatus must admit easily the tip of the index finger. Another modification is that I close the bladder in three layers making a completely air- and water-tight union. Features of Harris' original description which I should like to stress are:—first that the bladder should be empty before it is opened as not only is this procedure much simpler than opening it when full but it lessens contamination of the wound in cases where the urine is already infected; secondly, that the cavity left after removal of the prostate must be smooth and without tags or excrescences, in other words the enucleation must proceed through the line of cleavage and any tags must be excised; and thirdly, the trigonal stitch must be passed from immediately below and behind the mid-point of the inter-ureter bar and then brought forward under the floor of the prostatic cavity which it may enter at any point beyond, that is distal to, the edge of the trigonal flap. The object to be achieved is the fixing down of this flap and the idea that the suture must pick up the posterior edge of the torn urethra, whilst advantageous, is unnecessary. In connexion with the passing of this trigonal stitch two criticisms have been made. First, concerning perforation of the rectum, a catastrophe which I have never met nor have I heard of it occurring in other hands. I have heard fear of it expressed by many but I do not believe that its occurrence is possible if a correctly curved boomerang needle is used. Secondly, cases are on record where a ureter has been occluded by the trigonal stitch. I would point out that no operation is foolproof and that both ureter mouths must be visualized and the stitch passed at a point immediately behind the inter-ureter bar equidistant from the ureters. With this obvious precaution it is practically impossible to include or compress either ureter. Drainage should be by indwelling urethral catheter only but it is imperative to successful drainage that the catheter should be of 22 F gauge with an internal calibre of not less than 15 F. Its tip should be cut off after being passed and before closure of the bladder and it must be adjusted

(3) *Per-urethral resection*.—This method, in its present form, originated in America about 1930 and soon was acclaimed as the ideal treatment for all forms of prostatic hyperplasia. Not only were members of the medical profession swept off their feet by a wave of enthusiasm but the general public, having heard of the new method which obviated a "cutting operation", demanded it. Few now make use of it for every prostatic hypertrophy; most reserve it for the treatment of fibrous glands, the small subcervical adenomata and the case of obstructing carcinoma with impending or actual retention. In America the Mayo Clinic use it in preference to any other form of treatment and Emmett (1944) reports that for the ten-year period preceding 1942, 9,000 resections were performed there with a mortality rate of 1.1% and an average hospital stay of 8.6 days, only 3% requiring further resection at a later period for recurrence of obstruction. In England, Wardill (1947) also uses this method exclusively. He states that his cases are entirely unselected and that he has performed 537 resections during the twenty months prior to August 1947. 26 patients died (4.84%) and 58 required more than one resection (10.8%). On the other hand Millin (1946) after performing 219 resections discarded it, on account of late complications, except in the type of case I have specified. Chapman (1947) states that till recently he employed the method exclusively except for certain bad risk cases which were treated by permanent suprapubic drainage. He reports 379 cases with 24 deaths (6.3%). His present practice is to treat the large adenomatous prostate by suprapubic prostatectomy and 20% of his patients are now so treated.

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scar would fill many a plastic surgeon with envy. The only advantage of the long vertical mid-line incision is that a finger in the rectum is unnecessary (a matter of no importance) and visualization for spectators is somewhat easier.

Recently a good deal has been heard about patients suffering from bladder spasm following operation. After the Harris operation bladder spasm is almost abolished and certainly it is unusual for patients to complain of anything more than slight discomfort. The late results are perfect as I have determined by a yearly follow-up of 180 consecutive private cases over a thirteen-year period.

(5) *The Wilson Hey operation.*—In 1945 Wilson H. Hey advocated a revolutionary procedure. In cases of acute and chronic retention of urine he condemned slow decompression and urethral instrumentation as primary factors in causing infection with resulting post-operative uræmia. He advised immediate prostatectomy as being the best drainage operation and described his method by which, after enucleation of the prostate, the prostatic cavity was opened widely into the bladder by removal of the trigone up to the ureter mouths and inter-ureter bar, almost complete hæmostasis being effected by diathermy coagulation. He stressed the absolute necessity of passing the urethral catheter from the bladder outwards and of closure of the bladder wound if sepsis was to be avoided. The catheter is removed as soon as possible, usually about the third day. His operative technique is marked by the most strict aseptic ritual and he believes that by his method prostatectomy can be performed aseptically with resulting accelerated healing and that the urine, if sterile pre-operatively, remains sterile.

Hey classified patients into four groups relative to their condition at the time of operation. Group I were what he called perfect cases of any age with no marked systemic disease and residual urine up to 6 oz.—operation mortality 2.1%; Group II had mild systemic disease with residual urine up to 15 oz. and a blood urea of under 80—mortality rate 6.76%; Group III had marked systemic disease with residual urine of 1 to 5 pints and blood urea varying between 80 and 200—mortality rate 16.1%; Group IV all showed evidence of cardiorenal failure and had blood urea over 200—mortality 66.6%. Only 6 cases out of 335 were refused operation because death was too imminent. Over the whole series the operation mortality was 6% but in Groups I and II combined it was 3.4%.

After visiting Hey in Manchester I tried his methods but my experience of them is small. In the more serious cases (Hey's Groups III and IV) in which prudence indicated preliminary rest, restorative measures and slow decompression, 2 out of 4 patients died and I wondered if slow decompression and a two-stage operation might not have given a different result. For the ordinary prostate case (Hey's Groups I and II) the Harris operation to which I was accustomed gave better and more pleasing results in my hands so I returned to it. In spite of that I admire Hey's pioneer work. His conclusions regarding the dangers of sepsis from any form of bladder drainage must I think be conceded but in that connexion I cannot see how the retrograde passage of the urethral drainage catheter, on which he places stress, can have great bearing as *pre-existing* organisms in the urethra are going to ascend to the bladder sooner or later while a catheter remains in situ and thus it matters little whether the catheter is passed in the normal manner or as Hey recommends.

(6) *Retropubic prostatectomy.*—Millin (1945) was responsible for another revolution but this time mainly from the operative angle. He has described an extravesical method of prostatectomy which he has named retropubic prostatectomy and although he may not have been the first person to have thought of removing the prostate by the retropubic route he certainly was the first to devise a workable and relatively simple technique. The method he advocates has all the benefits of exposure and accessibility to the gland given by the perineal approach but is without the dangers of septic contamination and post-operative urinary incontinence inherent in that method. The operation has now been practised for two years and Millin has recently reported a series of 1,700 cases operated on by 16 surgeons, all of whom had carried out more than 50 operations, with an overall mortality rate of 5.3%. His own operative mortality in 439 cases is 4.75% (Millin, 1947a). It is as yet too early to dogmatize about final results but if Millin's present technique is carried out there would appear to be little chance of late complications. To one accustomed to prostatic surgery Millin's operation is not unduly difficult. My troubles concerned post-operative hæmorrhage and fistula. After completion of the operation I was surprised to note that the dressings required changing once or twice during the first six hours owing to their becoming saturated with blood. This occurred after every operation despite the most meticulous hæmostasis and despite the fact that no fall in blood-pressure had occurred during the operation. On only one occasion was it serious and that patient died of a sudden hæmorrhage into the prevesical space five hours after the operation in spite of the wound immediately being reopened and gauze packed and a rapid blood transfusion given. Generally I considered that there was a much greater blood loss from the prevesical drainage tube in the early post-

so that all its "eyes" will lie within the bladder and none within the prostate cavity as otherwise clot from the cavity may enter and occlude it; the position of the "eyes" is such as to secure adequate and immediate drainage of blood. I fix this catheter by a suture stitched to the wall of the catheter near its tip. One end of the suture is then attached to a large curved needle which should perforate the bladder wall from within at a point about 2 in. lateral to the line of the bladder incision where it is pushed through to the skin surface; the other end of the suture is similarly brought out on the skin surface on the opposite side. After closure of the abdominal wound a thin rubber tube, of a length sufficient to bridge the gap between the cutaneous exit points of the ends of the suture, is threaded on one end and the two ends are then loosely tied.

After closure of the bladder sulphathiazole powder is freely applied to the deep and superficial parts of the wound and also to the skin edges. A small tube is left to drain the prevesical space and the abdominal wall is closed around this by two silkworm sutures supplemented by a few Kifa clips. The wound is sealed by elastoplast over a few layers of gauze and this dressing is not disturbed for five days but a small hole in the centre of the elastoplast permits drainage from the prevesical tube and its withdrawal in forty-eight hours. Absorbent wool retained by a binder and easily changed covers the elastoplast. Finally the bladder is irrigated through the catheter and when the return is pink-coloured the bladder is emptied and 4 oz. of a 10% sodium citrate solution are instilled and the tube spigotted till the patient is returned to bed, following which 10 oz. of normal saline solution is administered rectally and the catheter connected to a bedside drainage flask by rubber tube. Later 1/6 grain of morphia is administered hypodermically. That is practically all the immediate after-treatment necessary but it is important that a nurse should watch that the urine continues to drip into the sterile bedside bottle. Irrigation of the bladder through the catheter is not permitted unless the urine fails to drip. If this should occur the nurse may force 2 oz. of saline solution, by means of a syringe, through the catheter and at once forcibly aspirate the amount inserted. If she fails to get a return the sister or house surgeon must be called but this is seldom necessary. Clot retention is uncommon and in most of the patients in which it has occurred it has been possible to clear the catheter by vigorous suction using a 2 oz. glass syringe. Where this fails, as it has on a few occasions, the catheter must be withdrawn, a Bigelow cannula inserted and the clot removed by an evacuator. I have found this method efficacious and in my experience it has never been necessary to reopen the bladder for clot retention. On the following morning patients treated by this operation feel and look well and are generally sitting up in bed reading their newspapers. Complications are practically unknown. The catheter is withdrawn whenever the urine is clear, usually in from six to eight days, and never later than the tenth day and following that natural micturition is re-established, the wound at that time having healed by first intention.

Patients after this operation may sit up out of bed in twenty-four hours but I never force a patient to get up against his will and usually he does not do so until the day on which the catheter is removed. The urine always shows some infection, generally a slight bacilluria following the operation but this can be cleared up in about a fortnight by treatment with sulphonamide.

The picture I have drawn is one which can be expected in any case where the general condition of the patient is fairly satisfactory and the urine sterile before operation. Where the urine is not sterile or where prolonged catheter or suprapubic drainage is required pre-operatively the urine takes longer to become sterile and a small quantity may leak through the suprapubic wound for a few days after withdrawal of the catheter.

I have found this operation with immediate closure of the bladder most satisfactory. I cannot understand why most surgeons still leave a suprapubic tube in the bladder as I believe that not only is that unnecessary but harmful. Fear of clot retention in the presence of a slight ooze from the prostate cavity is responsible for the practice but I would point out that a catheter such as I have described can clear the bladder of any trickle of blood and complete hæmostasis is unnecessary. During the past two years I have never failed to close the bladder at operation and I would go so far as to state that to-day any prostatectomy technique which entails leaving the bladder open even for a short period is undesirable.

There is one further alteration in Harris' original technique which has a considerable bearing on the comfort and rapid uneventful convalescence of the patient and which I regard as of importance and that is that the suprapubic wound should be small, transverse in direction, and situated one fingerbreadth above the pubis. After incising the skin and superficial fascia transversely, the linea alba is divided vertically from the pubis upwards for 2 in. The space thus gained when the recti are separated is amply sufficient for the operation. The opening into the bladder is made high and vertically and should not be larger than will admit the index and middle fingers. With a wound of this type the patient has no post-operative discomfort from his wound and the healing of the skin and subsequent

equally and that there is no gross hydronephrosis or hydro-ureter. (6) Renal function tests should not show a marked deficiency; a blood urea of 50 mg. % is regarded as satisfactory. (7) Urinary output should be about 80 oz. daily. (8) The cardiovascular apparatus should be found to be satisfactory on examination by a physician well cognizant of the amount of strain imposed by each of the possible prostatic operations.

Class II is made up of patients who do not qualify for Class I.—These patients are treated by urethral catheter drainage and are either quickly or gradually decompressed as may seem advisable. The majority of those who survive become fit for a closed method of prostatectomy within two weeks but if, at about that time, they have not done so then a suprapubic tube is inserted into the bladder and the patient is discharged from hospital. Such a patient is put under the care of his own doctor but attends our out-patient clinic at monthly intervals for re-examination. Whenever he shows improvement sufficient to allow prostatectomy he is readmitted and the operation carried out.

The principal hazard in the relief of prostatic obstruction occurs immediately after the patient commences treatment or even before treatment is instituted. Table IV shows this clearly and it proves that many patients are presented for treatment either at a late stage in the disease or even when death is already imminent. It provides a serious warning of the dangers of delay.

TABLE IV.—MORTALITY FROM PROSTATIC OBSTRUCTION

	Number	Died
Total number of consecutive cases admitted to hospital with prostatic obstruction.. .. .	260	31
A.—Treated by prostatectomy (all methods)	187	16
B.—Treated by drainage alone or receiving no treatment ..	73	15

Few patients who survive drainage fail ultimately to satisfy the criteria we consider necessary for safe prostatectomy and indeed our records show that, excluding prostatic carcinoma, less than 5% have been condemned to a permanent suprapubic tube. Commonly we have patients referred to us who have worn a suprapubic tube for months or years and have been refused prostatectomy elsewhere on account of their poor general or urinary condition. I believe there are few more distressing conditions for a patient than to be condemned to permanent bladder drainage and thus it often happens that such a patient will plead for relief even when fully aware of the considerable risk to life which, in his case, may be attached to radical operation. With careful pre-operative treatment it is surprising how many of these "elderly wrecks" can be given a new lease of life by a rapidly performed Freyer type of operation. A closure operation or any operation requiring more than ten minutes anaesthesia is usually unsuitable.

TABLE V.—PROSTATECTOMY BY ALL METHODS

<i>Private and Hospital</i>		
Prostatectomies (all methods)	Died	Mortality percentage
589	41	6.96

CONCLUSIONS

In the first place I should like to make it clear that in my opinion there is at the present time no single operative procedure suitable for all types of prostatic obstruction and I maintain that the type of operation should be adapted to the conditions presented by the patient. Many factors govern the choice, such as the condition of the prostate itself, the state of the urinary tract, the configuration and general health of the patient, his age and infirmities and especially the condition of his cardiovascular system. Thus it comes about that I view with misgiving the assessment of the difficult case by the surgeon alone; the prostate case can present such complex medical problems that if the best is to be done team work is essential and the team must include a physician experienced in the examination and treatment of this type of case. Another important factor in determining the type of operation is the "set up" of the hospital or clinic in which it is to be performed. It is wrong to undertake the treatment of prostatic obstruction except in a modern clinic where every aid, scientific, instrumental and human, is available. Except in dire emergency, a hardly conceivable condition in prostatic surgery, or in very exceptional circumstances, the urologist should refuse, for the reasons I have mentioned, to operate away from his own hospital clinic or nursing home. The general body of practitioners and the general public have such an experience of badly planned and performed prostate operations, with mortality in the region of 20% and a shocking morbidity, that the evil day of seeking or taking advice is deferred till conditions have so deteriorated as to make a perfect result unlikely. Only now with a better technique and better resources are we beginning to break through the

operative hours than occurred following the Harris operation. Other troubles from hæmorrhage occurred in cases where the bladder neck had to be resected widely. This resection left an opening into the bladder much larger than the catheter so that any bleeding from the prostate bed tended to ooze back into the bladder where it clotted and this often led to the catheter becoming blocked, and indeed on two occasions evacuation of the clots by the Bigelow evacuator was necessary. I have no doubt that this was the result of inefficient hæmostasis in the prostate bed and bladder neck and it shows the necessity for the identification and ligation or coagulation of all bleeding points. I cite this as a warning to those trying the operation. Another trouble was leakage from the suprapubic wound after withdrawal of the catheter. With a pre-operative sterile urine the suprapubic wound healed by first intention in all cases and after withdrawal of the catheter there was no ooze of urine from the wound but it was otherwise in some cases with a pre-operative bacilluria. These patients micturated normally after withdrawal of the catheter but most of them showed some leakage from the wound which persisted for from two or three days to as long as twenty days. In the same type of infected case treated by the Harris operation the fistula closed in a much shorter time. My nursing staff and my assistants concluded unanimously that the results we achieved by the Harris technique were on the whole better than by the Millin method. That finding may be peculiar to myself and detracts in no way from my admiration for this excellent method of prostatectomy and indeed I may, through later experience, use this technique more frequently.

The following table of my results with this technique is not a true reflex of the operation and only one death, which I have already described, can be attributed to the operation itself. At the time I was doing a series of retropubic operations I became temporarily imbued with Hey's teachings and I thought that if Hey's operation was suitable for use as a drainage operation in the very poor risk case with chronic overflow incontinence and high blood urea there appeared little reason why the retropubic operation should not prove equally satisfactory. Two of the deaths were accounted for by that view. The other deaths were due to coronary thrombosis in one and cerebral thrombosis in the other.

TABLE III

Type of patient	Number	Died	Mortality percentage
Private..	6	2	33·3
Hospital	24	3	12·5
Total	30	5	16·6

(7) *Perineal prostatectomy*.—This method of prostatectomy has never achieved popularity in this country although in America it had and still has a considerable vogue. Its main disadvantage is the possibility of urinary incontinence due to interference with the external sphincter. In the treatment of early carcinoma the route is a good one but the site of the wound is in an area exposed to septic contamination and thus the retropubic approach of Millin appears preferable (Millin, 1947*b*). My own experience of the operation is too small to be of any value.

(8) *The two-stage operation*.—By the two-stage operation I mean a preliminary cystostomy and bladder drainage as a first stage followed at a shorter or longer interval by removal of the prostate as a second stage. Any form of bladder drainage means urinary sepsis and thus it follows that, if at all possible, preliminary drainage should be avoided and post-operative drainage limited to the shortest possible time. Having admitted that, one has to consider the condition of the patient and his urinary tract and determine what will be safest and best for the particular case. The two-stage operation is undoubtedly a safer procedure for the inexpert but for the specialist the one-stage operation is in my opinion much to be preferred from all points of view. I find that I have performed a two-stage operation in approximately 6% of all cases.

METHOD OF SELECTION OF OPERATION

In my clinic in the Western Infirmary, Glasgow, we divide cases of prostatic obstruction into two classes:

Class I consists of those cases where preliminary drainage is unnecessary and a single stage operation can be safely performed.—The criteria we consider necessary for this are (1) There should be no palpable bladder distension or if distension is present it should not reach beyond a point midway between pubis and umbilicus. (2) The urine should not be grossly infected. (3) There should have been no recent urethral instrumentation apart from an indwelling urethral catheter. (4) Serious calculous disease should be excluded by X-ray examination. (5) Intravenous urograms should show that both kidneys are functioning

to various degrees of inactivation in the presence of some of the common organisms producing urinary sepsis, but in their absence it holds an important place and even in their presence may prevent pyelonephritis (Yates Bell, 1947) by acting as a remote barrier to the spread of infection. Either or both of these drugs should be used prophylactically and therapeutically. Their use has almost revolutionized prostatic surgery by removing fear of sepsis following the closure operations and already many report a very striking decrease in operative mortality (Yates Bell, 1947; Morson, 1947 *a, b*).

In cases where infection of the urine following operation persists after fourteen days of sulphonamide treatment, I give weekly courses of a mandelic acid preparation and sulphonamide alternately. This generally cures but in patients with a long history of prostatic obstruction and in whom pre-operative sepsis was marked the condition may be extremely intractable.

(3) *Suprapubic fistula*.—Reference to fistula formation following the Millin operation has already been made. Fistula following the Harris operation is uncommon. 77% heal by first intention, and in the remaining 23% healing is complete in about twenty days. In my cases no fistula persisted or required any form of secondary operation. In patients treated by the Freyer technique, where a suprapubic tube is used for drainage, fistula formation persisted for over fourteen days in about 75% of cases and in these the average time of closure was thirty days. No permanent fistula resulted from any type of operation and obviously such a condition persisting over months should not occur.

(4) *Post-operative urethral stricture*.—Reference has already been made to the incidence of severe stricture following per-urethral resection by the Thompson resectoscope; it is one of the great disadvantages of that operation. In no case did it occur after the Millin operation and in only a very few cases was there a minor degree of stricture following the Harris operation. Urethritis due to an indwelling catheter is also a common cause of this condition.

(5) *Incontinence*.—Incontinence following the Millin, Hey or Freyer operations has not occurred. Following the Harris operation a temporary total incontinence occurred in 1.4%. At first this puzzled me but cystoscopy showed it to be due to sloughing of tissue caused by over-tightening of the transverse sutures in the prostate cavity. This slough, about 1 cm. in diameter becoming partially impacted in the bladder outlet, interfered with sphincter action. The condition was completely cured with the passage of the slough which occurred naturally in all cases and caused no secondary hæmorrhage or after-effects.

(6) *Epididymitis*.—Every prostate operation should be preceded by bilateral vasectomy. This procedure takes four minutes and is done through bilateral small 1 cm. incisions in the scrotal skin. In no instance have these wounds failed to heal by first intention. In spite of this, epididymitis of minor degree has been known to occur but is uncommon. An inflammatory thickening of the cord proximal to the site of vas resection has occurred in 10% of prostatectomy cases in which there was marked urinary infection, but has gradually disappeared after a few days.

(7) *Urethritis*.—This rarely occurs post-operatively where there has been no pre-operative urethral drainage. If it does occur the catheter is at once withdrawn and intensive sulphonamide treatment instituted. In a patient treated by a closure operation where the catheter has had to be removed in the early post-operative period all the urine may be passed *per urethram* but, on the other hand, part may ooze through the suprapubic wound. Extravasation or serious complications have not occurred but a suprapubic fistula may form and may take a week or two to heal. Should urethritis develop during pre-operative drainage the catheter may have to be withdrawn and the operation performed by the two-stage method, but if intensive penicillin-sulphonamide treatment is instituted at once the infection may be aborted without necessitating removal of the catheter. Taken all over, urethritis has been uncommon in our hands largely on account of two factors, first, the institution of routine chemotherapy during the period of catheterization, and secondly because catheterization is performed with great care and gentleness. The catheter itself is anchored in position by the pipe-cleaner method, or a small self-retaining catheter of Foley type is used. Furthermore, while the catheter remains in the urethra a gauze dressing soaked in acriflavine 1:1,000 surrounds the glans penis and the first centimetre of the protruding catheter; this dressing is changed daily. Furthermore I believe it is important that the catheter should be a loose fit in the urethra to permit drainage of mucus, also that it should be held steady and not allowed to move: this is achieved by surrounding the penis with gamgee which along with the catheter is strapped to the thigh. While the catheter remains in the urethra the patient is not allowed to walk about although he may sit on a chair.

(8) *Pulmonary embolism*.—This occurred occasionally following all forms of prostatectomy till about two years ago. Only one case was serious, the patient dying within a few minutes on the third day following an open diathermy resection of a fibrous prostate. The others

crust of professional and lay resistance to early treatment and thus I maintain that there must be no setback in the position.

COMPLICATIONS AND SEQUELS OF PROSTATECTOMY

In recent years a good deal has been written about the complications and sequels of prostatectomy.

(1) *Hæmorrhage*.—(a) *At operation*: It seems hardly possible to perform prostatectomy without blood loss to the extent of from a half to one pint. Some patients bleed more than others but in all cases efforts must be made to minimize this loss. I have found that rapid but gentle enucleation of the gland, adhering rigidly to the line of cleavage with minimal tearing of tissue, limits the bleeding. Immediately the gland mass is freed and displaced from the prostatic cavity but before its removal from the bladder, I rapidly pack the cavity with gauze freshly wrung out of hot 1 : 1,000 acriflavine solution. This minimizes further bleeding while retractors are placed and the succeeding stages prepared. When all is ready the gauze is removed, any tags excised and the hæmostatic suture placed and tied. This takes five to ten minutes to accomplish and any further blood loss is trifling. I consider that this limitation of bleeding is one of the features of the Harris operation as I practise it and accounts for the lack of shock, rapid recovery and sense of well-being experienced by the patient within twelve hours of operation. Blood transfusion I rarely find necessary or desirable. In operations where bleeding is not fully controlled by suture, ligature or coagulation, a Foley type of catheter is useful. Recently attention has been focused on the use of "thrombin topical", and oxidized absorbable gauze, as hæmostatic agents in the prostate cavity. The former is injected into the cavity and the latter used as packing (de Vries and Buchanan, 1947) or as a covering for a dilatable bag (MacDonald and Powell, 1947). I have no experience of these hæmostatic agents in prostatic surgery and though they are probably unnecessary for the Harris, Hey or Millin operations, in transurethral resection or the Freyer operation they may prove of considerable value. Bandler, Roen and Stept (1947) have reported on 50 cases of per-urethral resection who received an injection of 10 c.c. of a solution containing 10,000 units of "thrombin topical" through an undistended Foley catheter into the prostate cavity immediately following the operation. Five minutes later the catheter balloon was distended and inserted into the cavity. The catheter was then clamped for one hour, after which it drained continuously. Irrigation was contra-indicated and unnecessary, post-operative bleeding being practically abolished. Chapman (1947) has used this technique in 36 cases, reports that irrigation is unnecessary and that the urine remains only blood tinged for a few days. He had no case of clot retention and he considers that the gain in comfort of the patient and convenience to the nursing staff was enormous. This means of eliminating bleeding may abolish most of the blood loss following the per-urethral and Freyer methods of prostatectomy, and it seems worthy of trial.

(b) *Reactionary*: The special No. 22 F rubber urethral catheter adequately drains off the slight ooze of blood which follows a Harris prostatectomy. The urine remains deeply blood-stained for twenty-four hours after which the hæmorrhage diminishes but as a rule it continues for four or five days—varying in degree from patient to patient. Clot retention following closure operations is rare and is best treated by removing the catheter, evacuating the clots by Bigelow evacuator and reinserting the catheter without necessarily removing the patient from his bed.

(c) *Secondary*: There appears to be some discrepancy in medical literature regarding the time of onset of secondary hæmorrhage. I would define it as hæmorrhage occurring from seven to fourteen days after operation and generally due to sepsis. I have found it to occur rarely, in fact my records show only 2 cases following the Harris operation. Both commenced a few hours after withdrawal of the catheter on the tenth day and in neither was sepsis a marked feature. Treatment by evacuation of the clot by Bigelow evacuator and reinsertion of a catheter for forty-eight hours was successful and convalescence was not delayed. When I say that the condition is a rare one I refer to massive hæmorrhage and not to a slight tinging of the urine with blood during the period within which secondary hæmorrhage might occur. This trivial secondary hæmorrhage is common and can be entirely disregarded, disappearing spontaneously within a few hours.

(2) *Sepsis*.—I do not believe that it is possible for any patient undergoing prostatectomy to escape some degree of septic infection. Indeed Riches and Muir (1933) reviewing all prostatectomy cases in the Middlesex Hospital between 1924 and 1931 found infection to be one of the commonest post-operative complications and the incidence of ascending infection to be appreciable. Recently Skyrme Rees (1947) has shown that over 50% of deaths following prostatectomy are due to severe sepsis in the urinary tract. The sulphonamides have proved of the greatest value in prophylaxis and treatment. Penicillin is said to be less useful owing

I think it is our duty as teachers to impress upon students the importance of making a digital examination of the rectum in as many patients as possible so that they may learn to distinguish the normal from the abnormal prostate, an art only acquired by experience. To the expert, diagnosis of prostatic carcinoma by rectal palpation is usually not difficult but I have been impressed by the frequency with which an obvious carcinoma has been missed by experienced surgeons; the reverse is equally true, and many cases labelled carcinoma have been proved to be non-malignant. Inflammatory conditions or calculi are often responsible for this error. Disturbance of the acid serum phosphatase is too uncertain to make it of value as a diagnostic aid. In many of my cases this has been found to be within normal limits when the patient had an advanced carcinoma of the prostate with multiple bone metastases. Statistics regarding the incidence and treatment of cancer are of no value unless the diagnosis is confirmed histologically. When a cancerous condition of the prostate is diagnosed by rectal palpation I am of opinion that even total prostatectomy will generally fail to avert a fatal issue and this applies equally to the more heroic partial excision of bladder, seminal vesicles, and prostate. In considering treatment for these patients one must bear in mind Morson's finding as a result of his experience in a large Local Authority hospital where patients may remain for years. He states that when treatment consists of nothing more than efficient nursing care and suprapubic drainage the expectation of life after diagnosis has been made is about three to five years (Morson, 1936). To provide efficient nursing care is difficult but if it can be secured one should consider whether the result likely to be achieved by a long and dangerous operation is worth while or the risk justifiable. The administration of stilboestrol often results in a shrinkage of the growth followed by natural micturition and thus operative procedures to relieve retention such as cystostomy or per-urethral resection may be delayed or avoided. It is my impression that the cases of carcinoma of the prostate likely to be cured are those in which the disease is buried within an adenomatous gland and in which the presence of the growth has been unsuspected and only proved at routine histological examination of the excised gland. It thus appears to me to be most unwise to perform the severe operation of total prostatectomy as a routine procedure on the chance that cancer might occur in that part of the prostate left after simple enucleation. Lowsley (1940) believes that total prostatectomy should be done more often than at present. He uses the perineal route and advises it in early cancer, chronic pyæmia, intractable chronic fibrosis, calculosis and certain cases of tuberculosis and adenoma of the prostate. In this country Anderson (1947) states that to those cognizant of perineal prostatectomy the operation is not difficult and the post-operative course is remarkably smooth but that there is a slight risk of incontinence. He has only done a very few cases and thus as yet is not in a position to form any conclusion as to its usefulness.

ANÆSTHESIA

The part played by recent advances in anæsthetic methods in relation to prostatic surgery has resulted in a considerable lowering of operation mortality.

At present I prefer induction by intravenous pentothal sodium, the anæsthesia being maintained with cyclopropane and minimal quantities of ether. Lately relaxation has been increased by the coincident use of d-tubocurarine chloride with excellent results, ether being omitted. Maintenance of normal blood-pressure during operation is of importance in any major procedure, but especially is this so in operations designed to permit immediate bladder closure, as more than a trivial fall in blood-pressure may obscure bleeding points resulting in subsequent hæmorrhage and clot retention.

Some years ago most prostatectomies were performed under spinal anæsthesia with coincident risk of a sudden and often uncontrollable fall in blood-pressure. With this method bleeding points, as already indicated, are obscured just when they should be visible and could be controlled and, in addition, the patient often exhibits signs of shock. Wilson Hey prefers spinal anæsthesia but emphasizes that it should never reach as far as the umbilicus, upward extension being controlled when light anæsthesia reaches a point midway between the pubis and the umbilicus. He maintains that if the anæsthesia is so restricted the fall in blood-pressure is minimal, 30 mm.Hg being the maximum permissible. I have found that the maintenance of such a level of anæsthesia presents considerable difficulty and much prefer general anæsthesia as described.

The anæsthetist must have opportunity to study each patient before operation with a view to assessing his general condition, fitness for the proposed procedure, and such factors as may influence the choice of anæsthetic. Generally speaking anæsthesia requires to be maintained for approximately one hour during which time the pulse should remain regular and the blood-pressure show little or no variation. There should be few after-effects; vomiting or nausea occurs in only a small minority of cases and chest complications are almost unknown.

were of trivial type, the embolus signifying its presence by a sharp pain in the chest and a rise in temperature, followed for a few days by a blood-tinged sputum; the condition resolved rapidly. Two years ago our consulting physician advised the administration of strychnine by mouth (5 minims of liq. strych. hydrochlor. dil. t.i.d.) for two days before operation, and for the days immediately following the operation that drug administered hypodermically, 1/30 gr. being given first followed by 1/60 gr. four-hourly during the succeeding twelve hours, after which administration by mouth may be resumed. Since then we have had no case of embolism, probably due to the effect of the strychnine on the circulatory and respiratory systems. In addition a knee pillow is forbidden and, on complete recovery from the anæsthetic, the patient is taught deep breathing exercises which are carried out at stated periods daily. He is also instructed to move about in bed and limb exercises are prescribed.

Recently articles have appeared in America describing prophylactic surgical treatment for a possible post-operative thrombosis. According to Allen (1947) any patient over 65 years of age who is to be confined to bed for some time should have bilateral superficial femoral vein ligation performed especially when a varicose condition of the veins of the leg exists. The even more drastic procedure of ligation of the inferior vena cava is recommended by Thebaut and Ward (1947) in the case of patients who have suffered one or more small pulmonary emboli. These procedures seem fantastic judged by experience in this country but conditions elsewhere may be different: surely as Bauer (1947) has stated, heparin or dicoumarol should prove equally effective. Prolonged operations probably encourage thrombosis and embolism, thus limitation of operation time is very important.

(9) *Osteitis pubis*.—4 cases have been reported by Yates Bell (1947) and 2 by Riches (1946). The incision which I employ for prostatectomy involves splitting of the linea alba right down to the pubes and possibly on occasion this might cause a wound of the periosteum which is thus exposed to infection from septic urine contamination but even so osteitis pubis has never occurred in my practice and thus Riches' suggestion that the condition is probably caused by lymphatic spread from a low-grade pelvic cellulitis may be correct. The condition is obviously one of some rarity and is likely to disappear with the more general use of chemotherapy.

(10) *Œdema of the penis*.—This occurs in a few cases following both the Millin and Harris operations. It may be due to interference with the venous return by sutures or ligatures which occluded tributaries of the deep dorsal vein, but as a rule rapidly disappears and is of little significance.

(11) *Meteorism*.—The occurrence of this condition following prostatectomy seems to be not uncommon in the experience of some urologists. I have only seen it in minor degree and it has never caused much trouble. Its occurrence may be the result of inefficient pre-operative preparation and the type of anæsthesia employed. The transverse incision and gentle treatment of the small part of peritoneum exposed at operation are probably factors in lessening its incidence and severity.

TREATMENT

(a) *Pre-operative*.—As the average age of the patient coming to prostatectomy is about 67 years his tissues generally show signs of deterioration and thus he cannot be treated as one in the prime of life. Irrespective of age or fitness I consider that he should spend two or three days resting quietly in bed, becoming acquainted with nurses and sick-room hygiene. A good night's rest in the new and strange surroundings is assured by the administration of a mild sedative and the strychnine, as described, administered. Intravenous urography, blood urea estimation, &c., are performed during this time. Cystoscopy or other urethral instrumentation should have been carried out previously or, if not, should be left till the patient is on the operating table where it can be performed immediately prior to the commencement of the operation. The surgeon personally must examine the patient and decide which type of operation is indicated. On no account must this be left to a house surgeon.

(b) *Post-operative*.—Post-operative treatment has already been described and I would only add that on leaving hospital patients are required to report at six-weekly intervals as I do not regard cure to be complete until the urine is sterile and micturition normal; this may be a policy of perfection not always achieved but it is nevertheless desirable.

CARCINOMA

So far I have dealt only with simple conditions of the prostate gland but unfortunately carcinoma of the gland is also a common cause of obstruction. Its incidence compared with simple enlargement is stated to be 1:5 but in my own experience it has been 1:6. Time does not permit a detailed consideration of this disease but I would like to make a few general observations.

I think it is our duty as teachers to impress upon students the importance of making a digital examination of the rectum in as many patients as possible so that they may learn to distinguish the normal from the abnormal prostate, an art only acquired by experience. To the expert, diagnosis of prostatic carcinoma by rectal palpation is usually not difficult but I have been impressed by the frequency with which an obvious carcinoma has been missed by experienced surgeons; the reverse is equally true, and many cases labelled carcinoma have been proved to be non-malignant. Inflammatory conditions or calculi are often responsible for this error. Disturbance of the acid serum phosphatase is too uncertain to make it of value as a diagnostic aid. In many of my cases this has been found to be within normal limits when the patient had an advanced carcinoma of the prostate with multiple bone metastases. Statistics regarding the incidence and treatment of cancer are of no value unless the diagnosis is confirmed histologically. When a cancerous condition of the prostate is diagnosed by rectal palpation I am of opinion that even total prostatectomy will generally fail to avert a fatal issue and this applies equally to the more heroic partial excision of bladder, seminal vesicles, and prostate. In considering treatment for these patients one must bear in mind Morson's finding as a result of his experience in a large Local Authority hospital where patients may remain for years. He states that when treatment consists of nothing more than efficient nursing care and suprapubic drainage the expectation of life after diagnosis has been made is about three to five years (Morson, 1936). To provide efficient nursing care is difficult but if it can be secured one should consider whether the result likely to be achieved by a long and dangerous operation is worth while or the risk justifiable. The administration of stilboestrol often results in a shrinkage of the growth followed by natural micturition and thus operative procedures to relieve retention such as cystostomy or per-urethral resection may be delayed or avoided. It is my impression that the cases of carcinoma of the prostate likely to be cured are those in which the disease is buried within an adenomatous gland and in which the presence of the growth has been unsuspected and only proved at routine histological examination of the excised gland. It thus appears to me to be most unwise to perform the severe operation of total prostatectomy as a routine procedure on the chance that cancer might occur in that part of the prostate left after simple enucleation. Lowsley (1940) believes that total prostatectomy should be done more often than at present. He uses the perineal route and advises it in early cancer, chronic pyæmia, intractable chronic fibrosis, calculosis and certain cases of tuberculosis and adenoma of the prostate. In this country Anderson (1947) states that to those cognizant of perineal prostatectomy the operation is not difficult and the post-operative course is remarkably smooth but that there is a slight risk of incontinence. He has only done a very few cases and thus as yet is not in a position to form any conclusion as to its usefulness.

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I have to acknowledge my indebtedness to Dr. J. A. W. McCluskie, Dr. W. B. Kyles and Dr. H. H. Pinkerton, physician, bacteriologist and anaesthetist respectively, for their co-operation and team work in the treatment of my cases of prostatic obstruction over a period of many years and to Mr. W. A. MacLennan and Mr. W. Laird Milne for their skilled surgical assistance and to Mr. A. I. L. Maitland for painstaking investigation of case records.

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[November, 27, 1947]

The following specimens were shown:

- (1) Carbuncle of Kidney; (2) Horseshoe Kidney (Right Half) with Pyonephrosis;
 (3) Renal Tuberculosis.—Professor R. J. WILLAN.
 Solitary Cyst of Kidney.—Mr. E. W. RICHES.
 Metastatic Abscess of the Kidney.—Mr. GEORGE LARKS.
 "Mixed" Kidney Shadows (Two Cases).—Mr. HAROLD DODD.
 Renal Hypoplasia.—Mr. ALEX. E. ROCHE.
 Calcification in Renal Tuberculosis (Three Cases).—Mr. J. H. CARVER.
 Duplication of Ureter in a Child of Nine Months with Ectopic Pyo-ureter.—Mr. J. D. FERGUSSON.
 Vesical Calculus.—Mr. H. WYNFORD JONES.
 Paraphimosis of the Clitoris.—Professor R. J. WILLAN.
 Large Adenomatous Prostate Removed Retropublically.—Mr. I. JACOBSON (for Mr. S. I. LEVY).

Section of Comparative Medicine

President—R. E. GLOVER, F.R.C.V.S.

[October 15, 1947]

The Influence of the Small Animal Breeder on Biological Research. [*Abridged*]

PRESIDENT'S ADDRESS

By R. E. GLOVER, F.R.C.V.S.

THE biological worker who is concerned with physiological or abnormal conditions both in the human and in animal species depends in no small measure on the quality of the animals available to him for experimental purposes. The breeder who provides the stock plays an important role since the conditions under which animals are raised in the breeding establishments may profoundly influence the results of the scientific worker. The various problems which confront the breeder are therefore bristling with interest and have not always received the attention which they merit.

As it is obviously impossible to cover more than a fraction of this field I have confined myself to three main sections dealing first with the care and maintenance of normal stock with special reference to the influence of diet on susceptibility and resistance, secondly with the influence of disease, particularly latent infections, on biological research and finally with steps which may be taken to co-ordinate and improve breeding animals.

General considerations.—The suitability of various types of buildings, cages, bedding, &c., was adequately discussed at two recent meetings on animal management (Farris *et al.*, 1945) (Biol. Methods Group, Soc. Publ. Analysts, 1947). It is scarcely possible to lay down exact requirements since the planning of buildings and equipment is a matter of individual taste: provided animal rooms are well lit, well ventilated and are easily washed down, cages are of adequate size and frequently cleaned and sterilized, and well-balanced rations are offered in a manner which prevents faecal contamination, an infinite variety of methods can be adopted. I would, however, stress the desirability of dividing animal houses into relatively small units. Admittedly there may be a slight increase in the labour required, but this is offset by the advantage of ease of isolation of stock into small units in the event of an outbreak of an epizootic.

The common diseases of small animals have been recently reviewed by Ratcliffe (1945) and by Parish (1947) who gave excellent advice as to the steps to be taken to secure their elimination. Special precautions may be necessary in the well-conducted Institute in which diseases have been avoided or are well under control since it is conceivable that in the absence of constant exposure to infection, highly susceptible races may develop. Ratcliffe (1945) has observed that: "Under natural conditions the species from which laboratory animals are derived are subject to many of the same infections that occur in captivity, yet they survive and multiply. One wonders, at times, whether or not efforts have been misdirected. Possibly colonies of laboratory animals should be fully exposed to infections, until by selection, highly resistant strains are obtained. Certainly, present-day efforts to exclude infection develop highly susceptible races." This ideal may sound attractive to the individual who is solely responsible for a normal breeding unit, but one may venture to doubt whether the experimentalist, who is frequently seeking the most sensitive animal, would be wholeheartedly in favour of uniformly resistant stocks. Such strains might be of value if resistance was highly specific for a particular group of organisms, e.g. *Salmonella*, and was "fixed" and invariable. There is no evidence, however, that "resistant" strains are not always undergoing modifications; moreover "resistance" is usually broad and may cover a variety of infecting agents. In the present state of our

knowledge it is probably wiser to adhere to strict quarantine measures and a constant laboratory check on incipient outbreaks of disease.

Diet.—It is highly desirable that the personnel responsible for breeding stocks should receive some elementary training in the compounding of rations and on the deleterious effects of ill-balanced diets. The present tendency is in the direction of cubed or pelleted foods which have advantages over wet mash and loose mixtures. They can be offered in wire baskets thus avoiding undue wastage, soiling with excrement is reduced to a minimum and provided they are prepared by a reliable firm, should give constant results. As far as this country is concerned particular attention may be drawn to the work of Watson (1937*a*) and Parkes (1946) who have provided useful data on fertility, weaning rates and growth of mice. Bruce and Parkes (1946, 1947; Bruce, 1947) have extended the use of pelleted food to rabbits and guinea-pigs; these diets contain such ingredients as bran, oats, barley meal, lucerne meal, &c. It must be stressed, however, that if it is desired to rear a colony on cubed food alone without the addition of any supplements of fresh food, it is essential to ensure that the ingredients are of the highest quality. There is an obvious danger that if a particular item is in short supply or is expensive, the manufacturers may be tempted to use a substitute material. The breeder should obtain a firm assurance that a compounded food will not be altered without notification and unless he can rely on such a guarantee he may run a risk of serious disturbances in his breeding stock which may well prove disastrous. For example, it has been shown under experimental conditions that the diet devised by Watson is satisfactory when it contains yeastrel. It was found, however, that if the yeastrel was replaced by an amount of dried yeast apparently equivalent to the yeastrel, there was a 50% drop in fertility in breeding mice within a few weeks while the young stock showed obvious signs of thiamine deficiency.

The problem of providing suitable pelleted foods for guinea-pigs and rabbits is more complex owing to the necessity for incorporating some form of green vegetation and in the case of guinea-pigs, vitamin C. Attempts to rear these species on purified diets suitable for rats have not been successful (Loosli, 1945). In the case of guinea-pigs the missing substances are present in fresh vegetation and a diet adequate in respect of protein, carbohydrate, &c., may not maintain growth unless supplemented with fresh green food. Bruce and Parkes (1947) reported, as we had noted in earlier experiments (Platt and Glover), that a good quality dried lucerne meal contains sufficient vitamin C to maintain the animals, but that when added to a compound ration and pelleted, the loss in ascorbic acid was often so high as to render the mixture inadequate to prevent scurvy. The former state that they can find no evidence that pelleted diets are deficient in any factor other than ascorbic acid. There are valid reasons for supposing, however, that the substances mentioned by American workers as "grass juice" factors are not a figment of the imagination. We have found that a synthetic diet composed of starch 64%; casein 24%; dried yeast 8%; salt mixture 4%; and vitamins A, D and E will give as good growth curves in guinea-pigs as "natural" diet provided a green-food supplement is added. The points to note are: (1) guinea-pigs fed on this mixture without lucerne meal die rapidly with symptoms of acute scurvy; (2) the addition of ascorbic acid improves the diet but growth is slow, reaches a peak and then declines, the animal eventually dying. There are signs of muscular dystrophy but no *macroscopic or microscopic evidence of scurvy*; (3) the addition of dried lucerne meal or of an autoclaved aqueous extract of green food gives normal growth curves; (4) amounts of lucerne meal as low as 2% may be adequate; since they contribute at the most 0.5% of protein to the diet, the protective effect is not due to protein deficiency in the basal ration; (5) autoclaved milk can delay the onset of death in guinea-pigs deprived of lucerne meal. The difference in activity of various samples of grass meal can be readily detected by feeding the meal at various levels.

Influence of diet on susceptibility or resistance.—Changes in diet which may affect the response of animals to various stimuli may be related to a restriction of diet in

which a condition of semi-starvation is enforced or to an imbalance of individual constituents. In so far as virus diseases are concerned, there is a general impression that the ill-nourished animal is less susceptible than the well-fed beast. A typical example is the variation in the response of rats, and to a less extent guinea-pigs, to foot-and-mouth virus whereby well-fed animals are much more receptive than are those in poor condition (Edwards, 1937).

Sprunt (1942), who reported that the reactions of rabbits to vaccinia virus were more pronounced in animals fed on a normal diet than in those which were semi-starved but given water, has postulated that the poorly nourished cell may be lacking in some of the materials necessary for the formation of new particles. In general, animals in poor condition show some increased resistance to viruses.

So far little evidence has been adduced that individual constituents of a diet can affect susceptibility to virus diseases. Experiments on low protein, or lack of vitamins A, D, and C, respectively, have failed to yield any concrete evidence that these elements play a significant part in the severity of a virus attack. There is a slight indication that the vitamin-B complex may be implicated. The experiments of Foster *et al.* (1944), Rasmussen *et al.* (1943) and others suggest that a depletion of the vitamin-B complex, particularly thiamine, may delay the action of murine poliomyelitis virus on the C.N.S. On the other hand, Zinsser *et al.* (1931) showed that rats which received a normal diet were resistant to the intraperitoneal inoculation of Rickettsiae but became much more susceptible if the vitamins were removed. It would seem, therefore, that the chance of establishing a virus in a laboratory animal might be significantly affected by the diet.

With regard to bacterial diseases there is some evidence that modifications in diet may influence resistance to infection, but unlike virus diseases, susceptibility seems to be enhanced when the diet is inadequate. This effect may be produced by withholding food; as, for example, the lowered resistance of starved mice to *Ery. rhusiopathiae* (Balfour-Jones, 1935).

There is also a general impression that animals receiving a diet grossly deficient in vitamin A are less resistant to both spontaneous and experimental infection (Drummond, 1919; Green and Mellanby, 1928; and others), but the evidence is not conclusive and has been disputed. In this connexion Webster and Pritchett (1924) who infected mice with *S. typhi murium* noted a death-rate of 15.9% when the diet contained 5% butter fat as compared with 77.8% with a fat-free diet. They were inclined to attribute the difference to the high vitamin-A content of their modified MacCallum diet but Watson (1937*b*) has pointed out that the ration also contained a high proportion of dried milk powder and casein: she was inclined to think that the vitamin A played a minor part in enhancing resistance. Certainly experiments of a similar nature carried out by Topley *et al.* (1931) were inconclusive in respect of the role of vitamin A in experimental infection.

The observations of Watson (1937*b*), Watson *et al.* (1938) are particularly interesting; they indicate that mice receiving a diet containing dried separated milk were more resistant to *S. typhi murium* than those fed on a ration free from milk. When exposed to infection by the "closed epidemic" method the percentage of survivors in the milk-fed groups were 56.3 and 75.5 as compared with 18.5 and 39.5 in the others. It is highly probable as suggested by Watson that the positive effect of adding or the negative effect of withdrawing a dietary constituent does not alter specific resistance to a bacterium or toxin but operates by influencing the well-being of the animals. Certainly no substantial evidence has yet been advanced that milk or any other constituent possesses any "anti-infective" factor in a restricted sense.

The necessity for very careful control of diets may have a special application in the standardization of biological products. Hartley in a series of classical experiments has shown that in groups of guinea-pigs fed on a basal diet plus ample cabbage there is a uniform rise in antibody to the injection of a diphtheria prophylactic, in contrast

to the wide scatter in groups receiving a supplement of mangolds and he attributed the difference to an effect of nutrition. The conflict of opinion on the effects of poor diets which in some instances appear to reduce and in others to enhance resistance to infection is difficult to explain. It is possible that the depletion of certain dietary constituents may act independently on the body cells and on the infecting agent. If the somatic cells are deprived of some essential factor and are thus partially "starved", their powers of resistance may be lowered to an extent which may render them more open to attack. On the other hand the virus or bacterium may suffer to a greater extent and possibly at an earlier stage so that in the poorly nourished animal, it perishes from inanition before it has a chance to become established.

In some instances, the passage of new agents to a host which is normally insusceptible may be effected by dietary changes. Thus, Glynn and Himsworth (1944) have set up a form of liver necrosis in the rat with diets low in casein and high in yeast. MacCallum and Miles (1946) have taken advantage of this liver damage and have shown that rats, which normally are completely unaffected when inoculated with the agent causing human infective hepatitis, develop hæmorrhagic lesions in the liver and glands if, prior to injection, they are placed on this methionine-cystine deficient diet.

Breeding stock may also be affected by the addition of deleterious substances to the diet. In one example which came to our notice, a group of 8-months-old guinea-pigs had failed to develop and many showed ascites; post-mortem examination revealed a generalized cirrhosis of the livers. It was then ascertained that several weeks previously the animals had received hay containing a high proportion of ragwort (*Senecio-Jacobea*). Six young guinea-pigs fed on this hay for ten weeks developed acute hepatic cirrhosis.

Changes in temperature can also exert a profound effect on stock. The optimum temperature in mouse and rat rooms is 65° F. to 70° F. and a drop in fertility and growth rates is liable to occur both at higher and at lower levels. Fluctuations in temperature are also liable to influence the response to various biological products, the susceptibility to transmissible neoplasms, nutritional studies, &c. In our own work (Platt and Glover) it has been found that the food intake in guinea-pigs placed on the synthetic diet supplemented with a dried grass meal already described (p. 86) and kept at 42° F. was much higher and the weight increase more rapid than in groups kept at 68° F. If, however, the grass meal was removed the animals at the lower temperature soon lost weight and died at a time when the controls were still in fair condition.

We have observed that mice, normally maintained at 65° F. and transported by van in substantial boxes with ample bedding (twenty-minutes journey) and then returned to a warm environment may show a fall in weight of 2 to 3 grammes in the next twenty-four hours.

It is evident, therefore, that the biological worker who is unable to raise his own animals and is dependent on stock derived from outside breeders should endeavour to maintain close contact with his source of supply. The results of biological research may be materially influenced if he is unaware of the diets offered by the breeder and of the conditions under which the animals are raised. Such information is rarely available in this country but recent trends in the standardization of manufactured foods and a closer control of breeding stock should lead to the raising of a more standard animal.

There is, however, another factor which must not be ignored. If a number of laboratories or individuals obtain a different end-point in the titration of a virus or the standardization of a biological product, it may be suspected, assuming that diet, external temperature and method of handling are identical, that there is some difference in the racial or genetical make-up of the experimental animals. Conflicting results may be avoided by selecting the same *strain*, e.g. Swiss mice, but there are obvious advantages in using inbred strains of proved homozygosity. There is a vast field for the development and wider use of pure-line strains raised under the supervision of a geneticist.

It would be a mistake, however, to rely entirely on such strains for all types of biological research since in some circumstances pure-line stock may be disadvantageous as, for example, when it is proposed by trial and error to attempt to establish a new agent. It is not unlikely that success will be secured if a mixed population showing all gradations of susceptibility and resistance is chosen in the hope that a sufficient number of reasonably sensitive individuals will enable the experimentalist to achieve his object.

Latent infections.—The types of infection which are responsible for a heavy mortality, e.g. *Salmonella*, are usually readily recognized. They may seriously interfere with biological research, but at least the investigator should recognize them and may be able to make allowance for their effects. Nevertheless, acute bacterial diseases of this nature sometimes tend to run in cycles and quiescent periods may be encountered when the stock is apparently unaffected. Occasional specific deaths will indicate, however, that infection is merely suppressed and that the disease is kept alive by "carriers" which are particularly dangerous because they are so difficult to detect. The rigorous slaughter of such suspected stock is probably the safest policy.

Equally insidious, although less dramatic in their effects, are the chronic infections, whose existence in "normal" breeding stocks may be quite unsuspected. For example, Sabin (1940) has observed that 80% of some mouse stocks carry pleuropneumonia-like organisms on the nasal mucosa or conjunctiva. Edward (1940) demonstrated that, in untreated mice, these organisms were quite harmless, but if the animals were anaesthetized and inoculated intranasally with any fluid, they might set up small pulmonary lesions, transmissible in series and liable to complicate attempts to isolate new agents. *Streptobacillus moniliformis* is also a common commensal. Wilson Smith (1941) isolated it from cervical abscesses in the Mill Hill stock of guinea-pigs, about 3% of which were affected. It was thought that infection might have been derived from rat-contaminated foodstuffs since Strangeways (1933) had already shown that up to 50% of the normal rat stock might harbour the organism in the naso-pharynx. It is interesting that following the complete elimination of the rat colony and its replacement by a stock which is apparently relatively free from infection, the disease has declined in the guinea-pig and has not reappeared.

The virus diseases which occur in small animals are even more insidious. The importance of latent infections was reviewed in the admirable Presidential Address given by Andrewes (1939) and these conditions confront the breeder with one of his most difficult problems. In mice, for example, infection with the viruses of murine poliomyelitis (Olitsky, 1940), mouse pneumonitis (Nigg, 1942), ectromelia (Marchal, 1930), grey lung virus (Andrewes and Glover, 1945), &c., may be widespread but may, nevertheless, be quite unsuspected. The mild infection of guinea-pigs with salivary gland virus (Cole and Kuttner, 1926), of rabbits with virus III (Rivers and Tillett, 1923) and of pigeons with ornithosis virus (Andrewes and Mills, 1943; Hughes, 1947) are also examples of latency.

A special stimulus may be required to reveal the presence of these agents but they are liable to assume a pathogenic character especially when animals are injected with heterogeneous tissues and fluids particularly by the intranasal route.

In the course of an investigation into porcine influenza an attempt was made to isolate a virus by serial passages of mouse lung from groups of animals receiving infected pig lung intranasally. Two strains of mice were used, one from a self-contained colony and the other derived from a commercial dealer. After three passages at three-day intervals, pulmonary lesions were detected in the close bred mice and were neutralized by specific serum. In the second group small areas of consolidation were seen after three passes and by the fifth passage many of the mice showed extensive lesions similar to those produced by Shope's virus. Serum neutralization tests with anti-influenzal serum failed, however, to inactivate the causal agent. It was eventually established that the mice were carrying ectromelia virus which became highly pneumotropic as a result of serial passage.

On another occasion an attempt was made to isolate a mouse pathogenic agent from throat washings, sputa and lung puncture material from suspected cases of primary atypical pneumonia in man. In both instances serial passages were negative but in a few cases slight lung lesions developed and the agent was identified as a mouse pneumonitis virus of the Nigg type. A latent virus of this type has been revealed in "normal stock" by the intranasal inoculation of sublethal doses of diphtheria toxin.

Most workers are fully alive to the need for great caution when attempting to adapt an infective agent to a heterozygous stock. They realize that the presence of mild infections capable of enhancement in virulence as a result of passage of tissues is so serious that stocks free from such conditions are extremely valuable. Unfortunately it is to be feared that they are all too rare. It is hoped, however, that breeders who possess strains which appear to be unaffected will take rigorous precautions to avoid the introduction of external infections by refraining from introducing fresh stock unless absolutely necessary.

The elimination of latent infections and their continued exclusion present one of the most difficult problems confronting the breeder and much research work will be required to devise satisfactory methods for their detection. Possibly the ultimate solution lies in the development of mutant strains with an increased resistance, but this is a long-term genetical problem requiring much patient work: alternatively, new discoveries in the field of chemotherapy may yield products which are active against these agents. In view of the sensitivity of Nigg virus to sulphadiazine, &c., it would appear possible that a course of drug treatment in breeding stock might achieve the elimination of infection existing in a latent form although, as far as is known, this method has not been tried.

Future developments.—In the past the raising of small animals for research purposes has too frequently been regarded as a side-line. It is true that there are well-organized units associated with large Research Institutes, hospitals or undertakings dealing with biological products, in which the breeding of normal stocks is conducted under proper scientific supervision. In general, these strains are dependable but naturally they can meet only a fraction of the demands of the experimental worker. A high proportion of animals used at the present time is drawn from commercial breeders and dealers, many of whom have no knowledge of the insidious effects of ill-balanced rations on fertility, rates of growth, &c., and are woefully ignorant not only of the dangers of introducing fresh animals without imposing a period of quarantine but also of the steps to be taken to limit outbreaks of disease when they arise.

One feels, therefore, that the quality of animals used for experimental purposes has not kept pace with the general advances in the field of biological research. This may be due in part to the fact that many Institutes are too small to warrant the establishment of an internal breeding unit and the research worker has to turn to commercial sources for his supplies. Even when a breeding colony has been set up, senior members of the staff have often been disinclined to devote sufficient time to the proper supervision of the stock which has been left in the hands of inexperienced and poorly paid attendants. Little improvement can be expected until it is clearly recognized that a high degree of skill and constant vigilance are essential to produce animals of the right type. The capital and maintenance charges of running such establishments are, of course, considerable, and the cost of each individual animal is probably appreciably higher than that obtained in the commercial market under normal conditions. I would add to this that whenever possible normal animals used for breeding should be completely divorced from experimental stock. This implies separate buildings and attendants for each class of animal and rigorous division of the two groups. The safest plan undoubtedly is to remove the breeding stock to a separate self-contained unit at some distance from the laboratory buildings.

It can be claimed that the experience of workers at the National Institute for

Medical Research and at other similar Institutes has shown quite clearly that the provision of a steady supply of suitable stock pays a handsome dividend. Fewer animals are required for critical experiments and the time of the investigator is saved since losses from intercurrent diseases are reduced to a minimum.

During recent years there has been a growing dissatisfaction with the stocks of unknown parentage, particularly in the field of animal nutrition. It is essential in trials of this type that variations due to genetic constitution, intercurrent infections, &c., should not obscure the picture. The case for reducing variability to a minimum has been put aptly by Hutt (1945) who says "when white rats of one strain gain only 14 grammes in five weeks on a diet low in thiamine, and those of another strain over twice as much, the interpretation of results is likely to be confused unless the two strains are in the one laboratory, and the difference, therefore, properly attributed to genetic differences between strain . . . rather than to variations in diets or in environment". This represents a rather extreme case, but the underlying principles are extremely important.

A most useful step was taken by the Conference on the Supply of Experimental Animals. One of the main tasks of the Standing Committee set up by the Conference was to circularize as many suppliers and users of small animals as was possible under wartime conditions. In its Memorandum the Committee forecast a considerable increase in the demand for animals for biological research and stressed that there would be a growing need for "healthy animals" produced under satisfactory conditions. It was strongly urged that in order to control animal supplies it would be necessary to set up some central organization to formulate policy and to act as a clearing house for information. It was suggested that the authority required for such steps should be vested in those Government Departments most intimately concerned with small animal supplies, *viz.* the Medical Research and Agricultural Research Councils, and the Ministry of Supply. This conclusion was reached largely as the result of the replies received from breeders and experimental workers. If mice are taken as an example of the frequency distribution it is found that some of the breeding establishments, both industrial and non-industrial, are breeding animals mainly for their own use although they are able to liberate surplus stocks to other users. There are also a few large-scale trading establishments breeding animals specifically for laboratory use. It is most significant, however, that there is an extensive number of small breeders. Thus if numbers of mice bred were grouped in suitable five- or tenfold multiples, it was found that 32% of the total number of breeders were each producing more than 2,000 mice per annum. The remaining 68% were all commercial units and were producing from 1,000 to 2,000 mice per annum or even less. It was ascertained that a high proportion of these small establishments were distributing stock through dealers. Such animals are often raised in poor surroundings and even if they are free from disease when they leave the breeder, they are liable to acquire infection in the hands of dealers. It was quite clear that the reason for the unsatisfactory conditions was the low price received by the breeder due in part to the profit taken by the middleman. Nevertheless the users are not without blame since so many Institutes fail to recognize that purchases in the cheapest market are not necessarily the most economical in the long run. The output from the large breeding establishments is at present insufficient to meet the demand especially in respect of guinea-pigs. Many Institutes rely, therefore, on the small breeders for their supplies. It is possible that the conditions under which the animals are maintained and distributed might be bettered through discreet propaganda but until the supplier can be guaranteed a satisfactory financial return, there is little hope of effecting a substantial improvement.

It is significant, however, that there is a tendency amongst large users to become self-supporting which will increase as the importance of guaranteed stock becomes more widely accepted and as bigger demands are made for stock for special purposes such as Friedman tests or cancer research.

The Conference recommended that a Committee embracing representatives of all interests concerned should be set up to formulate plans for the co-ordination of supply and demand, for the improvement of existing breeding units and the establishment of fresh centres if considered necessary, and for the development and maintenance of pure line strains, &c. It was also proposed that the collection of the necessary data should be vested in a Central Bureau which would act as a clearing house for information.

The Memorandum prepared by the Conference was submitted to the appropriate Government Departments. After due consideration, the Medical Research Council has agreed to set up an Advisory Committee and Central Bureau and has already taken the necessary steps. When the Bureau is finally established, one of its main tasks will be to renew contact with breeders and users. It is hoped that the breeders will supply full information as to the numbers and types of animals they are raising and thus enable the Bureau to set up a register of breeders—possibly at a later stage a register of accredited breeders. This information will be placed at the disposal of Research Institutes, &c., requiring supplies of suitable experimental animals. The success of the scheme will depend in large measure on the support which the Bureau receives from the two interests, *viz.* the breeder and the user. It is hoped that from time to time meetings will be held with Societies interested in small animal breeding at which the activities of the Bureau will be made known and the views of the biological worker ascertained.

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Section of Neurology

President—C. WORSTER-DROUGHT, M.D.

[October 2, 1947]

CLINICAL MEETING AT THE NATIONAL HOSPITAL, QUEEN SQUARE, LONDON, W.C.1.

Dermatomyositis.—J. ST. C. ELKINGTON, M.D.

Mrs. M. G., aged 29, was admitted to St. Thomas's Hospital 25.8.47, complaining of generalized muscular weakness.

History.—Previous health good except for an operation on her thyroid when 10 years of age. Family history—nothing relevant.

Present illness.—Four months before admission she developed a number of small superficial ulcers on her gums and inner aspects of lips and cheeks which coalesced and were very painful. They were accompanied by fever. Two weeks later her toes, arms, legs and back became painful and the limbs became generally weak. The arms were swollen for one week but after a brisk diuresis the swelling subsided. After two months the condition improved but on admission she still experienced difficulty in walking, generalized weakness of arms and legs, shortness of breath and some tendency to regurgitate fluids through the nose on swallowing, and headache.

On examination.—Temperature 98.7° F.; pulse 80; respiration 20. An erythematous rash was present on the butterfly area of the face, the back and front of the neck and the exposed area of the chest and the extensor aspects of the limbs. The affected areas were firm and sclerotic to palpation. There was a variable oedema of the eyelids and face. Numerous small white sclerotic plaques were present on the fingers. The thyroid was not enlarged.

Central nervous system: The cranial nerve functions were normal except for a slightly nasal voice. There was generalized wasting and weakness of the muscles of the limbs and especially those of the trunk with some tenderness on palpation. The arm reflexes were absent, knee and ankle jerks much diminished, abdominal reflexes absent and plantar responses flexor. No sensory disturbance was detected. The gait was "waddling" in character with marked lumbar lordosis and very reminiscent of that of a myopathy.

Investigation.—C.S.F. under normal pressure: 2 cells per c.mm.; Total protein 20 mg.%; Lange 0¹⁰; W.R. negative. Blood W.R. negative. Urine: Creatinine 116 mg./100 c.c.; creatine 46 mg./100 c.c.

Blood: Total protein 7.0; albumin 4.8; globulin 2.2; serum calcium 9.7; phosphorus 3.8; urea 27 mg./100 c.c.; cholesterol 240; alkaline phosphatase 1 unit.

Three successive twenty-four-hourly urine estimations gave:

(1) 1,200 c.c.	Creatinine 855 mg.	Creatine 400 mg.
(2) 1,320 c.c.	Creatinine 935 mg.	Creatine 545 mg.
(3) 1,520 c.c.	Creatinine 918 mg.	Creatine 538 mg.

Dr. F. Parkes Weber remarked that, although Dr. Elkington's case was quite a typical one in the sense that it showed the erythematous manifestations (notably of face) combined with obvious signs of involvement of striped muscle (a biopsy would doubtless have demonstrated degenerative

changes), it was not the most frequent type of dermatomyositis. The most frequent clinical examples constituted one of the most important groups of what Dr. Weber preferred to call "Symptomatic sclerodermas" (Parkes Weber, "Rare Diseases, &c.", London, second edition, 1947, p. 180). They were often diagnosed as examples of symmetrical sclerodermia, though the history of earlier erythematous, oedematous or febrile symptoms should make the diagnosis of dermatomyositis clear. Such cases, under general hygienic conditions with appropriate physical methods of treatment, tended slowly to improve, and occasionally all the sclerodermatous changes cleared up. Acute dermatomyositis, with generalized erythema, oedema and weakness, might prove rapidly fatal, and so also another rare type in young persons with severe myocardial involvement, somewhat suggesting acute rheumatic fever at first sight.

Lesion of the Brain-stem: ? Glioma of Pons and Medulla.—J. ST. C. ELKINGTON, M.D.

Mrs. J. F., aged 36.

History.—Ten months' difficulty in controlling L. leg, seven months' loss of use of L. arm and paralysis of the L. side of the face followed by difficulty in swallowing and talking. Deafness of the L. ear of doubtful duration.

Past history.—An acute illness at the age of 18 described as "sunstroke" characterized by intense occipital and frontal headache associated with sickness and some disturbance of vision. This illness lasted one month and since then the patient has been liable to frontal headaches.

On examination.—Mentally alert and co-operative but of less than average intelligence. Fundi, fields and pupils normal. Slight convergent squint. Complete loss of lateral conjugate deviation of eyes to R. and L. with preservation of upward and downward movements and of convergence. Nystagmus in looking up and down. Wasting of muscles of mastication (L.) with deviation of jaw. Diminution of sensibility to C.W. and P.P. L. forehead. Loss of L. corneal reflex. Loss of sensibility to pain and temperature R. half of face and scalp. Complete lower motor neurone paralysis L. face. Severe diminution of hearing and complete loss of vestibular function L. ear, the R. being then within normal limits. Severe weakness L. half of palate and pharynx, paralysis of L. vocal cord. Wasting and fibrillation L. half of tongue.

Motor functions.—Severe inco-ordination of cerebellar type with very coarse intention tremor in L. arm and leg without appreciable weakness.

Reflexes: Arm-jerks accentuated, knee and ankle jerks accentuated especially on the L. side. Abdominal reflexes absent. Plantars flexor.

Sensation: Loss of sensibility to pain and great diminution of temperature appreciation in the whole R. side of body. Postural sense and sensibility to light touch normal.

Skull normal. General medical examination revealed nothing abnormal.

Investigation.—C.S.F. under normal pressure: Normal in all respects; W.R. negative. X-ray of skull normal. No change in internal auditory meati.

Treated with deep X-ray therapy to region of brain-stem.

Progress.—Condition gradually deteriorating with the exception of the R.-sided analgesia and thermanæsthesia which has cleared up. In the last two weeks has become increasingly deaf in R. ear and vestibular responses are undergoing deterioration.

Thrombosis in the Sagittal Sinus.—J. PURDON MARTIN, M.D.

Mrs. E. M., aged 38.

Developed severe toxæmia in first pregnancy and was delivered on 5.6.47 following surgical induction of labour. Three convulsions occurred within five hours of

delivery, and there was no recovery of consciousness for twenty-four hours. She remained semicomatose for four days with no movement of limbs, and then had two fits which were mostly right-sided. Coma, complete flaccid paralysis and gross œdema followed, but recovery of speech started in twenty-four hours, and now all limbs have recovered and she is able to walk unaided. The paralysis was characterized by relative sparing of the hands and complete sparing of the face, which suggests that it was due to thrombosis of superior cortical veins, and as both sides were affected it is likely that the primary thrombosis was in the superior longitudinal sinus.

Painful Spasms of the Limbs: For Diagnosis.—DENIS BRINTON, F.R.C.P.

Mr. E. L., aged 62. Married ten years. No children.

History.—Deaf for many years (bilateral tympanic perforations). Psoriasis. No history of V.D. or head injury.

Present complaint.—Since August 1944 has had attacks of severe cramp-like pains in the limbs. Sometimes has trembled violently and fallen over. Tonic spasm usually begins in right leg, travels to right arm then left arm and left leg. Cries out with pain but no convulsions or loss of consciousness. Three years ago vision began to fail, especially in left eye. In past year has had "pins and needles" in both arms. Lately some stress-incontinence. Now has 10 to 20 attacks a day. Duration less than one minute.

On examination.—No obvious intellectual or emotional defect. V.A.R. 6/5 (corrected). Right disc pale. V.A.L.—hand movements only. Left primary optic atrophy and central scotoma. Left pupil reacts sluggishly to light. Limbs—no gross weakness but slight spasticity, ataxic gait, brisk tendon reflexes and doubtful extensor plantars. Sensation normal. Blood-pressure 110/74. C.S.F. normal. W.R. negative in C.S.F. and blood.

Calcified Aneurysm of Left Internal Carotid Artery (With Proptosis and Optic Atrophy).—S. P. MEADOWS, M.D.

L. W., male, aged 58.

History.—Seventeen years ago the patient developed severe pain in the left eye, followed, a few days later, by prominence of the left eye, squint and diplopia. The pain soon disappeared, but the proptosis and squint remained. Eight years ago he had a temporary recurrence of the severe ocular pain, and soon afterwards noticed that his left eye was almost blind. He has had two further attacks of severe pain in the left eye during the past year, lasting some weeks on each occasion, with vomiting, but with no dramatic change in the eye, and no loss of consciousness. During the last attack at Easter 1947 he noticed a sensation of "pins and needles" in the forehead and temple on the left side. There has also been increasing bilateral deafness during the past ten years.

On examination.—Marked left proptosis (about 4 mm.), but no pulsation. No bruit audible on auscultation of skull or eye. The left eye is blind, and the left optic fundus shows "primary" optic atrophy. Ocular movements of left eye very limited in all directions, except depression, which is almost full. Slight left ptosis. Left pupil of moderate size, fixed to direct light, but reacts slightly consensually. Left corneal reflex absent, and cutaneous sensation impaired over distribution of first division of left sensory fifth nerve. Bilateral deafness. Plantar responses extensor. No other abnormal signs in C.N.S. B.P. 120/85.

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Amyotrophy—Syphilitic.—COLIN EDWARDS, M.R.C.P.

Male, aged 50.

History.—Weakness of right fingers began insidiously in 1939. A year later he noted wasting and twitching of the right hand and arm muscles. Weakness of right leg followed with subsequent wasting.

1942: Admitted to hospital. C.S.F. analysis normal except for total protein of 60 mg.%. Blood W.R. positive. Impaired pain sensation was found over the right shoulder, arm and chest covering an area from C.4 to T.5 and considerable loss of tendo Achillis pain sensation together with wasting and fasciculation in the muscles of the right arm and leg, but there was no evidence of other sensory loss or of pyramidal involvement.

He was given intensive antisymphilitic treatment (chiefly with bismuth) for more than a year and then ceased to attend hospital until sent in recent months for review. He says that his condition has been quite stationary for the past two years.

Present condition.—There is now marked wasting of right hand, arm and shoulder girdle muscles with fasciculation there and in the other three limbs. Right leg wasted, right thigh slightly so. Tendon-jerks diminished in wasted limbs but only absent in markedly atrophic areas; left ankle-jerk absent, right very sluggish. Plantar reflexes flexor. Hypoalgesia to pin-prick over right segmental areas C.3 to C.8 and over the whole right lower limb. Loss of tendo Achillis pain sensation. Sensation otherwise unimpaired. Leukoplakia of the tongue is the only other abnormal finding.

Blood W.R. weakly positive but Kahn is definitely positive. C.S.F. normal except for protein of 60 mg.% and slight excess of globulin.

The President considered that the diagnosis was undoubtedly one of syphilitic amyotrophy on: (1) The relatively long history—eight years; (2) the fact that the condition had remained quiescent for at least the past two years; (3) the sensory abnormalities; (4) the fact that the amyotrophy is hypotonic rather than hypertonic; and (5) the positive Wassermann reaction in the blood. In many cases the cerebrospinal fluid shows no abnormality. Dr. Purdon Martin in 1924 had drawn attention to the predominance of the hypotonic type of muscular atrophy—rather than the hypertonic type—in syphilitic amyotrophy. A somewhat similar case was recalled by the President. This was a man who developed an amyotrophy affecting the right arm two years after the W.R.s had become negative; two years later he developed a Charcot arthropathy of the right shoulder-joint. Consequently in some cases even the blood W.R. may be found negative. Another example was that of a woman—the wife of a man with *tabes dorsalis*—who developed a muscular atrophy of hypotonic type affecting both arms and legs. She was first seen at the age of 50 and five years after the onset of muscular atrophy when the W.R. in both blood and cerebrospinal fluid was negative. She continued for a further twelve years without obvious deterioration (total course seventeen years) when she died from an intercurrent malady.

Spondylolisthesis with Cauda Equina Lesion.—N. G. HULBERT, M.D.

W. C., male, aged 69.

Present complaint.—Pain in the back and weakness of the legs.

History.—1940: At the age of 62, gradual onset of “pins and needles” in right leg which soon after became weak. In 1941, his left leg became affected, leading to difficulty in walking. He was admitted to a hospital, where apparently a diagnosis of motor neurone degeneration was considered. The legs gradually became weaker and he was admitted to the West End Hospital for Nervous Diseases in May 1944.

On examination.—His gait was unsteady, on a widened base, and he needed the support of a stick. Loss of power in all muscles below the knees but especially those of calf, with some wasting and hypotonia. Knee-jerks present and equal but ankle-jerks absent. Plantar reflexes flexor and abdominals present. Reduced sensa-

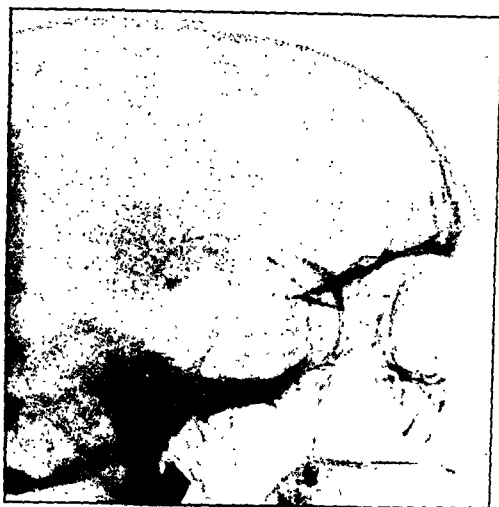


FIG. 1.

Calcified aneurysm left internal carotid artery with ring shadow above sella.

X-ray skull.—Large calcified ring shadow to the left of the sella, 4.5 cm. long by 3 cm. high. The margins of the left optic foramen are not visible, presumably due to pressure, and there is decalcification of the lesser wing of the sphenoid (fig. 1).

Percutaneous arteriography (Uriodone).—Appearances suggest a block of the left internal carotid artery just distal to the bifurcation of the common carotid artery. Although the needle appears to be in the internal carotid artery the contrast medium has run back and filled the external carotid artery.

This aneurysm probably originated in the intracavernous portion of the carotid artery, and rupture has been prevented by the dural sac of the sinus. The arteriographic findings suggest that the aneurysm has thrombosed (see similar calcified aneurysm, Meadows, S. P. (1934) *Proc. R. Soc. Med.*, 27, 1355).

Multiple Congenital Abnormalities.—DENIS WILLIAMS, M.D.

P. S., male, aged 14 years.

A case of maldevelopment of osseous, muscular, and subcutaneous tissue with central nervous system dysfunction as shown by intellectual impairment and dysphasia. There are electro-encephalographic and pneumo-encephalographic changes.

History.—The patient was apparently well until 11 months of age when he had measles followed by a constant right internal strabismus, a productive cough and radiographic evidence of pulmonary consolidation for two years. At the age of 2 years it was noticed that he had a deformity of the skull and scoliosis and that his joints were enlarged and limited in movement. He could not walk until the age of 3, after which he began to sustain closed fractures with minimal trauma. He had ten of these by the age of 11. He is ambidextrous but uses the left hand rather more than the right. He has had a slurring dysarthria and inco-ordination of fine movements since the age of 5 years. At the age of 8 to 10 it was found that he could not read or tell the time as well as the average child. He can handle figures visually or on auditory description; his most selective disability lies in comprehension of written symbols. No family history of similar complaint.

Dr. F. Parkes Weber suggested that the heading of Dr. Denis Williams's very interesting case might be altered from "Multiple Congenital Abnormalities" to "Amyoplasia (Hypomyoplasia, or Dysmyoplasia) Congenita, with Associated Abnormalities". The abnormalities associated with amyoplasia (Sheldon) differed widely in different cases. The association in this case might be termed "Denis Williams's type", whereas that in Dr. R. N. Herson's case (*Lancet*, 1947 (ii), 491) might be called "Herson's type". The secondary sclerotic process in the soft parts of the upper limbs in Dr. Williams's case, and the relatively slight secondary grasping posture of the hands, were insufficient to justify the term "Arthrogryposis multiplex congenita" (Stern). In regard to the generalized muscular defect the appearance of the whole thorax was very striking.

Clinical Section

President—G. E. VILVANDRÉ

[November 14, 1947]

Mikulicz's Syndrome.—F. L. KING-LEWIS, M.R.C.S., L.R.C.P., D.C.H.

Mrs. F., widow, aged 57.

History.—She has had intermittent swelling of both parotid glands, increasing dryness of mouth and a sore tongue for the past three years. On one occasion a small gritty particle was felt in Stenson's duct and later this passed into the mouth. For the past year she has had recurrent attacks of conjunctivitis and blepharitis, and more recently has noticed an inability to shed tears. There is nothing else significant in her past history, and no family history of any similar condition.

On examination.—There is chronic slight enlargement of both parotid glands and the submandibular glands are also palpable. Mr. J. H. Daggart has examined her eyes and reports the presence of keratoconjunctivitis sicca. Heart, lungs and abdomen normal. The liver and spleen not felt; no involvement of lymphatic glands. The blood-pressure is 180/95 and the urine is clear.

Investigations.—X-rays of the parotid glands show multiple small calculi; no sign of calculus in the ducts. X-rays of the lungs and hands show no abnormal changes.

Blood-count (November 1947).—R.B.C. 4,900,000; Hb 66% (Haldane); C.I. 0.67; W.B.C. 7,900, with normal differential count.

Treatment.—A culture was taken from the opening of Stenson's duct and penicillin-sensitive pneumococci were grown. A course of penicillin was therefore prescribed and 300,000 units in oil and beeswax were given, intramuscularly, twice daily for nine days.

The patient developed a severe urticaria at the end of this period. Sensitivity to potassium iodide was also shown on one occasion when this drug had been prescribed. A course of short-wave diathermy was administered to the parotid glands and although there appeared to be an improvement for a time this was not maintained.

The present treatment is entirely palliative.

Comment.—Mikulicz's disease proper is confined to cases in which there is swelling of the lacrimal and salivary glands and in which there is no involvement of the lymphatic system and a normal blood picture. It is probable, however, that many examples of Mikulicz's disease published in the literature have subsequently developed such changes.

The causes of Mikulicz's syndrome can be grouped under two headings: (1) The reticulosos and reticulo-sarcomata. (2) The granulomata.

Dr. F. Parkes Weber regarded the case as one of Sjögren's syndrome, that is to say, keratoconjunctivitis sicca, with swelling of the parotid salivary glands and dryness of the mouth as striking (though non-ocular) features. Such symptoms, at all events in early stages, might be intermittent or remittent. In his paper on the non-ocular features of Sjögren's syndrome (*Brit. J. Ophthalm.*, 1945, 29, 299) Dr. Weber had not alluded to any case like the present one, with minute salivary calculi as a (? secondary) complication. From the symptomatic point of view Dr. King-Lewis's case might of course also be termed one of Mikulicz's syndrome, though not Mikulicz's disease.

tion to light touch and pin-prick over buttocks and back of thighs, extending nearly to popliteal space on left and half-way down thigh on right. Tendo Achillis analgesia, and vibration sense much reduced in legs. Some hesitancy of micturition: anal and bulbo-cavernosus reflexes both present. Anus slightly patulous. Heart normal with blood-pressure 140/80.

X-rays showed pronounced spondylolisthesis, the dorsum of sacrum being almost at right angles to axis of spinal column; fifth lumbar vertebra wedge-shaped with apex posteriorly. The cerebrospinal fluid showed no abnormality, with pressure 85 mm., total protein 35 mg.%. W.R. negative in cerebrospinal fluid and blood. A myelography with lipiodol showed the lipiodol column to end at the upper border of the first sacral segment.

On May 30, 1944, laminectomy (Mr. G. C. Knight) was performed. The fifth lumbar vertebra lay about 1 cm. deeper from the surface than its normal line. It was displaced quite considerably in relation to the fourth lumbar vertebra, but it was only slightly depressed and rotated in relation to the first sacral segment, the maximum displacement being at the upper border of the lamina. The laminae of the fifth lumbar and first sacral were excised. The theca seemed to be kinked on the posterior aspect beneath the fifth lumbar lamina at its junction with the first sacral segment, but Mr. Knight was not convinced that this really caused compression, as the anterior face of the neural canal was entirely smooth, without any projection of the vertebral bodies which might distort its lumen. There was a considerable pad of fat beneath the junction of the fourth and fifth lumbar vertebrae.

The patient's condition has remained much the same excepting that the calf muscles have become weaker and more atonic. November 1946: The cerebrospinal fluid again showed no abnormality. Lumbosacral support gives no apparent benefit.

Comment.—First, was the lesion, as seems probable, one of the cauda equina rather than of the conus medullaris; second, was the gross spondylolisthesis the cause of the cauda equina lesion, or if it were coincidental what alternative cause could be assigned for the condition? It was suggested that the spondylolisthesis might be causative.

In reply to a question raised regarding possible involvement of the fourth and fifth lumbar roots, as shown by the wasting of the gluteal muscles, it might be suggested that the gross displacement shown on the X-rays could well cause compression or tension of the fifth lumbar root, while the first and second sacral roots are also concerned in the nerve supply of the gluteal muscles.

In reply to a further question there was no history of trauma.

POSTSCRIPT. Since the case was shown, further examinations on the X-ray tilting table have suggested some narrowing of the lipiodol column in the region of the first lumbar vertebra, and a further laminectomy is contemplated.

This case was shown on account of the uncommon nature of the gastric tumour and because it demonstrated the ease with which resections involving the uppermost part of the stomach can be performed when using an abdomino-thoracic incision. This approach is well tolerated even by elderly patients and does not necessarily entail a more complicated convalescence than a purely abdominal intervention.

Severe Diabetic Neuropathy with Right Phrenic Palsy.—E. MONTUSCHI, M.D., and G. MELTON, M.D.

N. H., male, aged 57.

Past history and family history.—Nothing relevant. Married, with two sons.

History of present complaint.—Glycosuria discovered in 1943. Stabilized with diet and insulin at Prince of Wales Hospital, Tottenham. In November 1944 required higher doses of insulin—40 units Z.P.I. and 40 units S.I. November 1945: Onset of cramps in legs and weakness in both legs and right arm. Much worse in March 1946, with severe weakness and dimness of vision, loss of weight and anorexia. No bladder dysfunction. Admitted to Prince of Wales Hospital in May 1946. Findings as follows:

Diabetic retinitis in right eye. Wasting of shoulder-girdle muscles on the right. Severe wasting of muscles of both legs, with vasomotor changes in the feet. Bilateral foot drop.

Investigations.—Blood-count normal; diabetes apparently well controlled. Wassermann negative. C.S.F. contained 325 mg. of protein and no excess of cells. Skiagram of chest normal. E.C.G. normal.

Transferred to Northern Hospital on 19.6.46. Progress has been very slow, but good, and he can now walk with the aid of toe springs and sticks. Slight paresthesiae in right upper limb, with uncertainty in writing. No sphincter disturbances, but impotence. The requirements of insulin have diminished. Now on S.I., 30 and 44 units daily, with glycosuria well controlled.

On examination.—Amblyopia right eye, right pupil smaller than left; reacts sluggishly to light but well to convergence, and dilates only half-way with atropine. Marked neuro-retinopathy on the right, less marked on the left. No wasting of shoulder girdle. Good motor power in both upper limbs, with no demonstrable sensory loss. Supinator, biceps and triceps jerks present but weaker on the right side. Superficial abdominal reflexes present. Lower limbs—good glutei. Some wasting but fair power of extensors in both thighs, better on the right. Severe wasting of muscles of leg on both sides, with complete foot drop. Right knee-jerk present, left absent. Ankle-jerks absent. Plantar reflexes not obtained. Complete sensory loss over distal part of the feet. Sensory loss less marked over lateral aspect of legs. Glossy skin, vasomotor and sudomotor palsy over the feet and distal part of the legs. C.V.S.—Heart normal, B.P. 115/90, dorsalis pedis and posterior tibial arteries easily felt on both sides. Respiratory system.—Poor air entry and diminished respiratory excursion at the right base.

Investigations.—Blood-count normal. Fractional test meal shows high acidity curve. Blood sugar estimations and urinalysis charts show moderately severe diabetes well controlled by insulin. Blood cholesterol 208 mg. %. W.R. negative in the blood and C.S.F. Repeated investigations of C.S.F. show raised protein, now 60 mg. %, Lange's curve normal, pressures normal, and Queckenstedt's test shows no spinal block. Skiagrams of chest from July 1947 show paralysis of right dome of diaphragm, with slight paradoxical movement. Screenings confirmed by double exposure film on 30.9.47. Skiagram of cervical spine showed no abnormality.

Comments by Dr. E. Montuschi.—Diabetic neuropathy of the severity of the present case has been repeatedly described in the literature, but a marked polyradiculitis, with raised protein in the C.S.F. and an Argyll-Robertson pupil, are not common. We can find no reference to phrenic palsy in diabetic polyneuritis, although it has been described in alcoholic and other toxic neuropathies. There are no clues to any other aetiological agent but diabetes in our patient.

Polycythæmia Vera. Hypertensive Heart Disease. Erythromelalgia Syndrome and Osteoarthropathy in the Right Leg.—G. MELTON, M.D., and E. MONTUSCHI, M.D.

Housewife, aged 58. Symptoms of polycythæmia and hypertension first appeared during 1938. Frequent venesections at London Hospital in 1939. Symptoms of circulatory failure for past two years.

October 1946: Complained of increasing pain, burning, sweating and swelling in right leg, particularly when walking. Admitted to Northern Hospital in May 1947.

Leiomyosarcoma of Stomach. Thoracico-abdominal Gastrectomy.—FRANK FORTY, F.R.C.S.

H. W. P., male, aged 66.

History.—For the past two months the patient had noticed that his food seemed to stick at the level of the lower end of the sternum. Swallowing was difficult and painful. He had lost some weight.

On examination.—No abnormality was found.

Barium swallow.—Barium was held up at the cardia. There was slight dilatation of the œsophagus. There was a large filling defect between the lower end of the œsophagus and the barium-filled body of the stomach. The appearances indicated a large proliferative growth of the cardia.

Operation (22.5.47).—Regional block plus gas, oxygen and ether anaesthesia. Exploration of the abdomen through an upper left paramedian incision disclosed that the growth was mobile and that there were no metastases. The incision was extended transversely through the left rectus muscle and the chest opened along the eighth left intercostal space, the costal margin divided and the diaphragm split. The upper half of the stomach and lowest inch of the œsophagus were resected. The œsophagus was anastomosed to the body of the stomach in the left pleural cavity. The chest was drained through the ninth interspace and the incision closed.

Post-operative progress.—There were no complications. A barium swallow one month after operation passed down the œsophagus without delay or difficulty and there was no obstruction at the site of the anastomosis. The patient left hospital five weeks after operation.

The specimen.—A sessile, slightly lobulated tumour occupies the fundus of the stomach and projects into the lumen. The mucosa over the tumour is smooth and not ulcerated. The margins of the tumour are well defined (fig. 1).

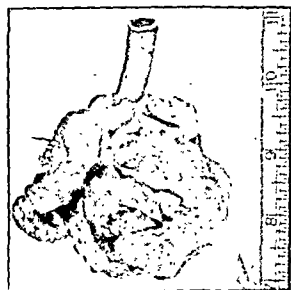
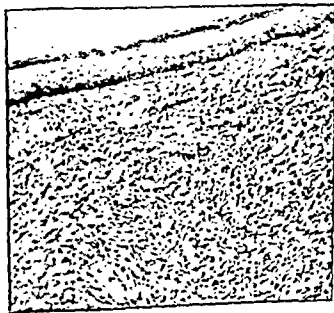


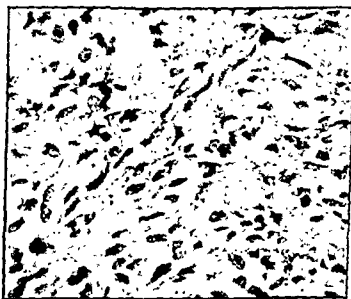
FIG. 1.

Photograph of operative specimen showing the tumour. The rubber tube marks the junction of the œsophagus with the stomach.

Histological report.—Tumour composed of fasciculæ of spindle-shaped cells separated by thin layers of collagenous tissue. The muscle immediately underlying the mucosa is compressed but not invaded. Within the tumour there are strands of cells indistinguishable from ordinary smooth muscle and the close connexion of the tumour cells with these suggests that they arise from them. The irregular nuclear size and hyperchromatism of many of the neoplastic cells suggest a degree of malignancy although mitosis is infrequent (fig. 2) Diagnosis: Leiomyosarcoma of low-grade malignancy.



×90



×420

FIG. 2.—Photomicrographs of the tumour. See description in text.

II.—Trans thoracic Vagal Section for ? Recurrent Anastomotic Ulcer.

Mr. H., aged 54.

History.—Symptoms of duodenal ulcer commenced in 1929, when aged 38, and continued until 1944, when a gastro-enterostomy was done at another hospital. The pain returned two weeks after operation. Severe diarrhoea developed in April 1947, accompanied by loss of weight. In July 1947 laparotomy showed a gastro-jejuno-colic fistula. Partial colectomy and partial gastrectomy with posterior gastro-jejunostomy were performed.

22.10.47: Patient readmitted complaining of recurrence of pain.

Night secretion test showed abundant free acid in every specimen except one. Histamine test and insulin test showed a similar high response. On 28.10.47 gastroscopy—no anastomotic ulcer seen. However, it was felt that this patient might well be going on to form another anastomotic ulcer with its attendant dangers.

5.11.47: Trans thoracic vagal section was performed through the left eighth intercostal space, dividing the ninth rib posteriorly. The left and right vagi were ligated proximally and 1½ in. of each were removed down to the oesophageal hiatus.

Post-operative convalescence was uneventful.

24.11.47: Night secretion test showed complete achlorhydria. There was slight response to histamine showing the presence of acid-producing cells in the stomach, but insulin test gave a negative response, indicating complete section of the vagi.

Mr. R. C. B. Ledlie said that these cases illustrated the profound effect produced on the gastric secretion soon after vagus resection. The first case showed the value of estimating the night secretion and the insulin test in determining whether the vagus resection was complete. An abdominothoracic approach had been employed to overcome the anticipated technical difficulties from adhesions in dealing with a gastro-jejuno-colic fistula after three previous gastrectomies. It was of interest to note that the pleural cavity did not become infected although the operation necessitated closure of an opening in the colon. This might well have been due to the use of sulphasuxidine and penicillin.

Cloquet's Hernia.—H. FREEMAN, F.R.C.S.

H. C., a male, developed a large right inguinal hernia following an operation for appendicitis in 1933. In 1941 he noticed a small globular swelling in the left groin which gradually became bigger yet remained painless. The swelling extended into the upper part of the thigh; he can push it upwards until it disappears, and it seems to be controlled by a truss.

Cloquet's hernia, or pectineal hernia as it is sometimes called, was first described in 1777 by Callinson and later by Cloquet in 1817. It is a variety of femoral hernia, but instead of descending from the femoral canal through the saphenous opening and cribriform fascia, Cloquet's hernia passes more medially, not through the saphenous opening, but over the pectineus muscle through the loose connective tissue and into the thigh, where it is separated from the skin by subcutaneous tissue only and may even descend as far as the knee-joint.

Mr. Duncan Fitzwilliams said that Cloquet's hernia was a rare condition. In this case it was replaced with remarkable ease, but he thought he could feel a small finger of omentum which was adherent low down in the sac, which did not reduce and which caused re-descent on the slightest exertion.

Malignant Melanoma of Eyelid with Secondary Deposits in Regional Lymphatic Nodes.— REGINALD A. KING, F.R.C.S.

Mrs. E. G., aged 45.

Four years ago a pigmented mole on the left lower eyelid began to enlarge. It was treated by silver nitrate cautery by her doctor.

July 1947: A recurrence on the same eyelid was partially removed for section by an ophthalmologist. Pathological report: Malignant melanoma.

August 1947: Wide excision of lower eyelid with plastic repair.

November 1947: Pre-auricular and post-auricular nodes enlarged and increasing. Small nodule of growth on lower lid. Abdomen and chest normal. X-rays of chest normal.

Suggested treatment.—Excision of lower eyelid with enlarged lymph nodes and intervening lymphatics *en bloc*. Facial hypoglossal nerve anastomosis.

Mr. Duncan Fitzwilliams said that he thought the idea of a block dissection of the growth, the lymphatics across the cheek, and the glands of the region was not a wise procedure. Theoretically it was correct perhaps but this procedure was not followed in the case of cancer of the tongue or of melanotic growths—for instance in the foot. It was considered enough to make a wide excision of

On examination.—Clinical picture of polycythæmia vera with typical appearance, gross splenomegaly and characteristic blood picture. There were also signs of hypertensive cardiac failure, mainly left-sided.

Right leg larger than left; characteristic appearance of erythromelalgia, being warmer and redder than the left; sweating of right foot with marked pulsation of the dorsalis pedis and posterior tibial arteries. The skin temperatures confirmed the warmer state of the right leg.

X-rays: Right leg—tibia, fibula, and metatarsals were broadened and showed periosteal thickening characteristic of osteo-arthritis. X-ray of chest shows marked cardiac enlargement and signs of extensive pulmonary congestion at both lung bases.

Blood-count.—R.B.C. 8,400,000; Hb 156%; W.B.C. 23,700; Polys. 95%. No primitive cells; platelets 1,750,000.

Progress.—Deep X-ray therapy June and July. Blood-count on 9.7.47: R.B.C. 7,300,000; Hb 140%; W.B.C. 21,000; platelets 285,000. Spleen markedly smaller; below this could be felt a mass which, on intravenous pyelography, was confirmed as being the left kidney. The pyelography shadow was normal. There had been albuminuria, together with a *B. coli* urinary infection, in July, which cleared up on sulphonamide therapy. Cardiac failure abated. Symptoms and signs in the right leg much improved and there is now no evidence of erythromelalgia. However, the X-ray appearances are unchanged.

Comment.—Erythromelalgia has been frequently described as a complication of polycythæmia vera, and on several occasions it has been noted as being unilateral, as in the above case. We have been unable to find any record in the literature of unilateral osteo-arthritis associated with erythromelalgia as a complication of polycythæmia vera. We consider it probable that the osteo-arthritis has arisen as a result of the chronic pulmonary stasis with secondary infection in the lungs, and that the localization in the right leg was probably determined by the abnormal peripheral vascular changes in the limb.

Dr. F. Parkes Weber, in discussing the erythromelalgia-like syndrome in the right lower limb (which had already almost subsided), referred to the case of a Rumanian woman, aged 36, with typical splenomegalic polycythemia, who had recovered from an acute erythromelalgia-like attack in the feet (chiefly the left foot). She also had arterial hypertonia (F. P. Weber, *Med.-Chir. Trans.*, London, 1905, 88, 191).

Dr. Weber did not think that the X-ray appearances in the present patient's right leg were like the typical symmetrical changes in true cases of pulmonary osteo-arthritis, but he drew attention to H. Batty Shaw's account of changes of the kind in heart disease—compare Batty Shaw and Stanley Melville, *Proc. R. Soc. Med.*, 1917, 10, Clin. Sect., page 8; Batty Shaw and R. H. Cooper, *Trans. Clin. Soc., Lond.*, 1907, 40, 259; L. F. Barker, *Intern. Clinics*, 40th series, 1930, 3, 54.

[December 12, 1947]

TWO CASES SHOWN BY D. P. CHOYCE, F.R.C.S., FOR R. C. B. LEDLIE, F.R.C.S.

I.—Abdominothoracic Approach to Recurrent Gastro-Jejuno-Colic Fistula with Section of Vagi.

Mr. E., aged 53.

History.—1935: Perforated duodenal ulcer. 1936: Polya type partial gastrectomy for cicatrized duodenal ulcer. 1938: Operation for anastomotic ulcer. Further strip of stomach removed and new anastomosis made. 1941: Another anastomotic ulcer adherent to colon. Fistula undone and anterior gastro-jejunostomy performed. Left subphrenic abscess and left empyema had to be drained during convalescence.

1941–1946: Epigastric pain after meals continued. One hæmatemesis in 1946.

September 1947: Readmitted complaining of epigastric pain and recent diarrhœa.

1.10.47: Right transthoracic vagal section.

19.10.47: Patient losing ground. Night secretion, histamine and insulin tests showed abundant free acid, indicating that section of the vagi had not been complete.

29.10.47: *Final operation*—abdominothoracic approach. Gastro-jejunocolic fistula separated into components. Holes in colon and jejunum closed. Anterior gastro-jejunostomy performed. One and a half inches of vagi excised at œsophageal hiatus.

21.11.47: Good recovery. Night secretion and insulin tests show almost complete achlorhydria, indicating complete section of the vagi.

Section of Dermatology

President—J. E. M. WIGLEY, F.R.C.P.

[October 16, 1947]

Epidermolysis Bullosa Acquisita.—H. W. BARBER, F.R.C.P.

Male, aged 42. Agricultural labourer. Married with one normal child aged 11. Three brothers and two sisters alive and well. One sister died in childbirth. No history of any comparable disease in the family.

Eruption appeared four and a half years ago as "small blisters" on lower abdomen. Other parts including buccal mucosa affected later. Lesions dried into scabs, leaving "scars" on which new blisters appeared after traumatism. At that time trauma did not produce lesions on normal skin. The condition was diagnosed as *pemphigus* and he was admitted to the local hospital, where the skin healed, but relapsed on some areas soon after discharge.

16.8.43: First seen by me. Diagnosis: Dermatitis herpetiformis with buccal lesions. Characteristically grouped urticarial papules and bullæ were then present. Cleared temporarily with sulphapyridine. Seen again 4.12.44. Grouped lesions still present and single bullæ of some size. Diagnosed as transitional case between dermatitis herpetiformis and pemphigus. No suggestion then of epidermolysis bullosa, nor when in Guy's Hospital 11.8.45–1.11.45. Treated with blood transfusions, sulphapyridine, and fourteen three-day courses of stovarsol. Discharged greatly improved. Seen again 25.7.46. In the meantime iodide had been given and had apparently provoked new lesions.

14.9.47: Readmitted to Guy's Hospital. Had done no work for two years. Clinical picture completely changed. Raw or crusted lesions, some of considerable size, chiefly at pressure-points over bony prominences and on folds of skin liable to tension, e.g. axillæ and antecubital fossæ. Skin of hands and feet atrophic and papyraceous with bullæ or their remains. Buccal mucous membrane affected by recurrent blisters leaving painful raw areas. Diagnosis of *epidermolysis bullosa acquisita* made. The majority of bullæ are subepidermal, others apparently under the stratum corneum.

Investigations.—Urine: No albumin or sugar. Calcium oxalate crystals.

Blood-counts.—15.9.47: Hb 72%; R.B.C. 4,200,000 per c.mm.; C.I. 0.86; W.B.C. 10,000 per c.mm. Differential count: Polys. 64%, eosinos. 9%, basos. 1%, lymphos. 24%, monos. 2%. 1.10.47: W.B.C. 8,400 per c.mm. Polys. 70%, eosinos. 4%, basos. 1%, lymphos. 22%, monos. 3%. Serum chloride 268 mg.%. Serum sodium 360 mg.%. Urinary excretion of chloride within normal limits.

Biopsy.—The skin shows separation of the epidermis from the dermis by œdema fluid and is devoid of inflammatory disease. Elastic fibres are scanty or absent below the bullæ.

the growth and to remove the glands of the region; the lymphatic vessels were left alone. Most people recognized that inadequate treatment of the small growth by the cautery usually only stimulated the growth and was like stirring up a wasp's nest with a stick. He thought in this case the excision should be wide and it might be found that this had to include excision of the eye.

Diabetic Neuropathy and Hepatomegaly.—R. N. HERSON, M.B. (introduced by Dr. N. LLOYD RUSBY).

H. N., male, aged 64.

First seen February 1947. Sugar first found in urine ten years previously, but he had not kept to a diet or received insulin regularly.

On admission.—Urine loaded with sugar, acetone+. Immature cataracts; pupils did not react to light or accommodation. Arteries thickened, B.P. 180/100. Left foot gangrenous. Knee and ankle jerks absent. Chronic *B. coli* infection, resistant to sulphonamides. Blood sugar controlled on a diet of 200 grammes carbohydrate, 80 grammes protein, 80 grammes fat, and 25 units soluble insulin morning and evening. The gangrene was treated locally and with intramuscular penicillin. He was discharged at the end of August.

Readmitted in October, with bilateral ptosis which had developed suddenly after three weeks' severe continuous frontal headache. Epigastric discomfort and flatulent dyspepsia. Sallow complexion, slight yellow discoloration of sclerae. Liver 3 fingerbreadths below costal margin, smooth, firm and not tender.

Eye movements almost absent. Pupils small and fixed. Corneal reflexes present. Remainder of cranial nerves intact. Right biceps-jerk present, other arm-jerks absent. Upper abdominal reflexes obtained, not lower. No weakness or inco-ordination of lower limbs. Knee and ankle jerks absent. Right plantar response equivocal, left could not be elicited because of deformity of foot. No loss of appreciation of touch but pin-prick could not be felt below middle of legs. Responses to heat and cold irregular. Complete loss of vibration sense in legs, no loss of position sense. Dr. Blake Pritchard considered the dissociated sensory loss could only be explained on the basis of a central lesion, the oculomotor palsies and loss of tendon-jerks being consistent with diabetic neuropathy.

Investigations.—Urine: Alkaline; protein 0.012%, sugar varying; urobilin, slight excess; bile pigments trace; bile salts nil; a few erythrocytes and a large number of leucocytes. Culture: *B. coli*.

Blood: Hb 90%; R.B.C. 4,750,000; M.C.V. 86.3 c. μ ., W.B.C. 12,300 (polys. 54%, lymphos. 31%, monos. 12%, eosinos. 2%). Blood urea 39 mg.%. Blood W.R. and Kahn negative. Blood sugar curve: Before sugar 364 mg. per 100 c.c., after thirty minutes 400; sixty minutes 570; ninety minutes 500.

C.S.F. Clear, colourless; protein 90 mg.%, chlorides 730 mg.%.

22.10.47: Van den Bergh, direct weakly positive in half a minute, indirect 1.7 mg.%. Total protein 6.87, albumin 2.76, globulin 4.11 grammes%. A/G ratio 1/1.5. Alkaline phosphatase 72 units, gold test + 3, thymol turbidity 14 units. Serum cholesterol 285 mg.%.

Test meal: High normal values for total and free acid.

X-ray examination: Pituitary fossa normal in size, contained a few small flecks of calcium. Slight ventricular enlargement with some widening of aorta. Only osteoarthritic changes in lower spine and pelvis.

Progress.—Headache soon ceased but ptosis remained in spite of treatment with thiamine. In order to allow patient to see, one lid was strapped open during the day but after a week an ulcer appeared. The opposite upper lid was strapped open with similar result. Apart from constipation he had no abdominal symptoms, and general condition improved slightly. Jaundice difficult to detect. Serum tests on 2.12.47: Van den Bergh direct positive in three minutes, indirect 0.8 mg.%. Total protein 5.47, albumin 2.70, globulin 2.77 grammes%. A/G ratio 1/1. Alkaline phosphatase 32 units, gold test +5. Thymol turbidity 20 units. Thymol flocculation 4+.

POSTSCRIPT (6.2.48).—During the last two months there has been a very gradual improvement, the left eye is now a third open and the right a quarter.

in a paper read before the American Dermatological Association, but not yet published, stated that tocopherols are beneficial in certain dermatoses in which collagen metabolism seems to be disturbed.

Dr. H. W. Barber: I have had a good many cases of this kind. The first point is whether one agrees with Ormsby in considering lichen sclerosis as being distinct from atrophic lichen planus. I feel that, clinically and histologically, the conditions are distinct. The majority of cases in which I have diagnosed lichen sclerosis have been women after the menopause, and usually it has affected what I call the menopausal areas—the vulva, the neighbouring parts of the groin and buttocks, and the submammary and axillary regions. I have treated some by oestrogens given by mouth, but two or three cases by local applications of either 2·5 of 5% dienoestrol cream. It is of interest that vitamin E has been advocated for disturbances of the menopause.

Dr. R. M. B. MacKenna: With regard to the vitamin E question, I am using vitamin E entirely experimentally and am very conscious that I have not got the preparation of vitamin E that I require. I have in two cases seen women with lichen sclerosis associated with pruritus vulvæ, as described by Dr. Elizabeth Hunt. In these cases 3 mg. of α -tocopherol four times a day were given, and in that non-significant number of cases the women have returned after a short period and have said that the pruritus had completely disappeared. The possible action of the drug is a complicated matter: probably it is associated in some way with endocrine biochemistry and requires yet some considerable research. J. F. Burgess of Canada, who has done much original work on the use of tocopherol in disorders of the skin, says that chronic lupus erythematosus, granuloma annulare and possibly scleroderma and lichen sclerosis may be beneficially influenced by large injections of mixed tocopherol—100 to 300 mg. every day. We cannot get this synthetic preparation over here, and α -tocopherol, which we can obtain, is not very suitable for injection intramuscularly, because such bulky doses have to be given that the buttocks are made very sore.

Case for Diagnosis. ? Poikiloderma of Civatte.—R. T. BRAIN, M.D.

Mrs. B. L., aged 38, was seen for the first time to-day and gave a history that she first noticed a pigmented area on the left cheek about three years ago. The colour varied a little from time to time but the area extended and before long the pigmentation affected the other cheek. Her periods began at 13 and have been regular, lasting three to five days with some pain on the first day. No skin reactions to menstruation have been noted. She has two sons, aged 12 and 16. The only medicine she takes is senna, but she has constantly used a cosmetic cream on her face.

On examination.—The patient is in good general health and is blonde with a pink complexion. The abnormal feature is a patchy brown or brownish-red macular pigmentation affecting her cheeks, particularly at the sides of her face, extending slightly to the neck. Many fine telangiectases are seen amongst the pigmented macules which produce a coarsely mottled pattern with a finer reticulated character in some parts. It is thought that a few minute areas of atrophy are present in the pigmented areas but the degree of atrophy is slight. About the temples, especially on the right side, the follicular openings are unduly patent but do not show the coarse plugging suggestive of lupus erythematosus.

Although this patient presents many of the features attributed to the variety of poikiloderma described by Civatte it is believed that these features are not essentially different from those described in some cases of Riehl's melanosis which have been ascribed to contact with mineral oils and tar. This patient has used the same face cream constantly and the opinion of members is sought as to the possibility of her pigmentary dermatosis being the result of the constant application of this oily product which contains some paraffin and various aromatic oils, including oil of bergamot. Somewhat similar cases seen in the last few years have appeared to be more dependent upon contact with greasy preparations than to be related to some endocrine disturbance, as was originally suggested by Civatte, and one has had little success with the treatment of such cases by hormone therapy, although Dr. Barber and others have reported successful treatment with oestrogenic hormones in characteristic cases of Civatte's syndrome.

Comment.—A case was recorded by Dr. MacLeod (*Brit. J. Derm.*, 1931, 43, 420) of acquired epidermolysis bullosa affecting the hands only in a man aged 50. The condition was then of four years' duration. He had a remission in the winter of 1930 lasting until May 1931, during which time he had been able to use his hands freely—sailing, gardening, &c. There was no apparent explanation either of the remission or relapse.

I have recently had under observation for a long time a similar case—a man aged 67—who also had ichthyosis, which had become more severe of late. Some of the earliest bullous lesions occurred in the larynx and Mr. Scott-Brown suggested the diagnosis of pemphigus, with which I at first concurred. The buccal mucous membrane was severely involved, and eventually the clinical picture became very similar to that of the present case. Investigations and various treatments proved of no avail.

Dr. J. T. Ingram; I have had two cases of this type. One was a woman who was aged 44 when the condition started, and it continued for about twelve or thirteen years when she appeared to recover. It was mostly on the hands, with more damage to the nails than in Dr. Barber's case, and some epidermic cysts were present. The other patient was a man whom I had under my care for several months in hospital, and he had been affected for ten years. He was then 44 or 45 years old, and he had not worked for eight years. He also had severe mucosal lesions and developed spontaneous bullæ. He died eventually from bronchopneumonia. I have been very interested to see Dr. Barber's case.

Lichen Sclerosus et Atrophicus treated with Vitamin E.—R. M. B. MACKENNA, M.D., and BRIAN F. RUSSELL, M.D.

Mrs. J. A., aged 58.

November 1946: She noticed a white spot in the right groin and later in the left, which she attributed to an emotional disturbance.

April 1947: The condition spread to the axillæ.

May 1947: It spread beneath the breasts with severe itching.

June 4, 1947: The condition became worse following a bereavement.

She also complains of sharp pains in the groins and much mental depression, with excessive sweating at the time of onset but not since the condition has developed. Her last menstrual period was at the age of 43.

On examination (April 1947).—White, atrophic and patchily pigmented, slightly infiltrated plaques on the anterior and inner aspects of the thighs, also on the right buttock and in the axillæ, less marked under the breasts. Mucosæ normal.

Treatment.—She received treatment with diœstrol, phenobarbitone, and unguentum alcoholium lanæ, without apparent improvement. Since August 6 she has been treated with vitamin E (α -tocopherol) one 3 mg. capsule three times a day.

The lesions now appear much more supple, particularly the axillary and sub-mammary lesions, but biopsies taken from the lesion on the left thigh on April 18 and October 1, 1947, show no appreciable dissimilarity. They both show an atrophy of the epidermis with some increase of pigmentation in the basal layers, fibrosis in the upper part of the dermis, and an occasional perivascular collection of chronic inflammatory cells.

POSTSCRIPT.—The patient developed a seborrhœic type of eruption on the trunk, controlled by salicylic acid and sulphur, following her attendance before the Section.

Comment.—Vitamin E (a mixture of α and β -tocopherol) is said to control the production of œstrins if given in excess. Of these, α -tocopherol is thought to be the anti-sterility factor and β -tocopherol is thought to supply myotropic and neurotropic factors. Good results have been claimed in myopathic conditions. Recently Burgess

in a paper read before the American Dermatological Association, but not yet published, stated that tocopherols are beneficial in certain dermatoses in which collagen metabolism seems to be disturbed.

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Dr. A. C. Roxburgh: There were a number of cases in Brazil or Argentina some time ago during the war which were ascribed by the man who wrote the paper to the use of inferior cosmetics. He said that among the passengers on a bus or tramcar one could find several people every time with this pigmented condition of their faces. The South American races no doubt pigment more easily than we do.

The President: I have seen a number of such cases and am still very much of the opinion that the external application of some oily or greasy agent is an important factor. In one case, "patch testing", without exposure to light, produced no erythematous reaction at all, but simple pigmentation.

Dr. H. W. Barber: Apart from the pigmentation, two essential features of Civatte's condition are telangiectasia and slight atrophy. I do not quite understand how cosmetics could produce these two changes.

Dr. Theresa Kindler: I think most of the original cases described were in women. In 1924 Kerl published a survey of 17 cases from the Clinic Riehl of which 2 were men, 2 children, the rest women of various ages, mostly in domestic occupations.

On the question of external or alimentary causation, Riehl and his school thought that the disorder was caused by a toxic agent contained in the war bread. They separated it from Hoffmann's and Habermann's melanodermatitis toxica, which is caused by external irritants such as tars, mineral oils, and kindred substances. Riehl considered the absence of inflammation and the involvement of the scalp to be distinctive symptoms of his disease. Most other workers think that the two conditions are identical or closely related, and that both alimentary and external toxic agents, by producing a sensitization to light, are responsible for the disorder. The poikiloderma Civatte also is usually included in this group.

Dr. W. N. Goldsmith: Pigmentation attributed to petroleum, coal, and tar first aroused interest during World War I, when lubricating oils and other derivatives were used in a crude state, especially in Germany and Austria. Thus, in 1917, Oppenheim described a case of intense, brown-black discoloration of the face and neck from lubricating oil. In the same year Riehl published his cases, which were at first attributed to the ingestion of other food factors, and later possibly to petroleum used as a constituent of margarine.

The President: It is not without interest that at the time Riehl's original papers were published, describing the condition as war melanosis, there was considerable malnutrition amongst the population with whom he was dealing. I think we have seen more cases recently than we saw during the period before the war, and it is a fact that there is not as good nutrition in this country as there was. This may be a factor as well as the oils. In some cases there seems to be no possibility whatever of oil absorption.

Dr. Henry Corsi: I read Riehl's original paper, which was published in 1917. He assumed in it that the condition was due to malnutrition. Later on that idea was abandoned by everybody, including Riehl, and the condition was believed to be due to an external irritant. Riehl's cases were nearly all men, but not exclusively so. The physical signs were a large amount of pigmentation, but scarcely anything else. In the present case there is a change in texture and a poikiloderma, i.e. a variegation in pigment instead of mere increase, which was the main feature of Riehl's cases. It does not seem to me therefore that the present case can be classed as one of Riehl's type of pigmentation; it is more closely allied to the poikiloderma of Civatte.

Dr. W. Lemberger: In addition to pigmentary anomalies there are in quite a number of cases certain hyperkeratotic excrescences on the back of the proximal phalanges. The condition does not consist of pigmentary anomalies alone.

Other cases were shown as follows:

Lichen Planus in Linear Distribution.—Dr. J. D. EVERALL (for Dr. L. FORMAN).

? Lichen Planus.—Dr. C. H. WHITTLE.

Granuloma Annulare with Extensive Lesions.—Dr. R. M. B. MACKENNA.

Darier's Disease.—Dr. D. WEITZMAN (introduced by Dr. J. E. M. WIGLEY).

Total Alopecia treated with Thorium X (Four Cases).—Dr. P. J. FEENY.

(1) **Leucoderma and Leucotrichia.** (2) **Erythema Induratum and Papulonecrotic Tuberculidè.**—Major J. MORGAN, R.A.M.C.

Keratoderma Blennorrhagicum.—Dr. G. B. MITCHELL-HEGGS, Dr. J. J. KEMPTON and Dr. M. FEIWEL.

... to be published later in the *British Journal of Dermatology*.)

[November 20, 1947]

(?) Eczematoid Tuberculide.—H. W. BARBER, F.R.C.P.

Dr. J. S.

History.—An eruption appeared on the left hand September 1946. In November 1946 a radiograph of the chest revealed evidence of tuberculosis of the apex of the left lung and for this he has been under the care of Dr. E. R. Boland. The left hand was treated by X-rays with success. In May of this year he ran a splinter into the right palm and at this point the existing eruption appeared and spread to its present extent. Treatments with lotions and ointments were apparently ineffective. He has been under the care of Dr. Erskine until quite recently, and at the latter's suggestion he consulted me.

Eruption.—The patient is an ichthyotic. There is a vesicular eczematoid dermatitis involving the greater part of the right palm with sharply margined borders. Although it is unilateral, the appearances do not suggest a dermatitis from an external irritant. In view of the history I thought the possibility of an eczematoid tuberculide had to be considered, and a patch test with tuberculin jelly was performed on the left forearm. This provoked an acute vesicular eczema with a few pustules. Control test negative. As with other positive patch tests, the fact that the epidermis is sensitive to the substance applied is, of course, not proof that the substance in question is responsible for the existing eruption but, in the absence of any other apparent cause, it seems to me likely that in this patient the palmar eczema is due to epidermal sensitization to tuberculin; in other words an eczematoid tuberculide.

In 1920, Attwater, Marshall and I (1921) described a series of cases of an eczematoid dermatitis, occurring almost exclusively in children and adolescents as scaly patches of a characteristic fawn or pale brown colour, usually dry, but sometimes oozing—probably as a result of scratching or rubbing—and situated chiefly on the extensor surfaces of the limbs, the trunk, and on the face, particularly on the temples and forehead below the margin of the hair. In about 80% of the cases described Marshall and Attwater were able to demonstrate definite signs of active tuberculosis. I christened the eruption "dermatitis scrofulosa." Dowling and I (1926) described a further series of cases, and we showed that (1) exactly similar patches may arise *de novo*, and persist for some time in tuberculous children at the sites where von Pirquet's test with tuberculin has been done, and (2) in children with dermatitis scrofulosa, patches identical in appearance and histological structure with those already present may be produced by applying tuberculin to the skin. We also observed cases of undoubted lichen scrofulosorum, in which patches of dermatitis scrofulosa were coexistent, and put forward the view that the latter is an eczematoid variety of the former. I am also of the opinion that the so-called "fausse teigne d'Alibert" is in some cases dermatitis scrofulosa occurring on the scalp.

Some years ago a child whom I had treated in infancy for eczema was brought to me for scaly patches on the limbs and trunk, which were characteristic of dermatitis scrofulosa, accompanied by slight generalized enlargement of the lymphatic glands. The practitioner in charge of the case was entirely sceptical of my opinion that the child had active tuberculosis, but a week later there occurred an outbreak of typical lichen scrofulosorum, and the late Dr. J. J. Perkins confirmed the diagnosis of tuberculous adenitis.

Hügel, Eliascheff, and Schaumann (1927) have recorded cases of lichen scrofulosorum in which the normal papular eruption was associated with "brownish red scaly patches of psoriasiform aspect". Schaumann found in microscopical sections infiltration with epithelioid and giant cells around the follicles.

Comparable to dermatitis scrofulosa is, I think, the eczematoid trichophytide described by Jadassohn and Guth, and the eczematoid microsporide of Finnerud (1925). It is generally agreed that they are varieties of the lichenoid trichophytide or microsporide, just as dermatitis scrofulosa may be regarded as a variety of lichen scrofulosorum. I believe that these eczematoid eruptions are due to the sensitization of the epidermal cells to the toxins, tuberculin and trichophytin respectively, and the artificial production of dermatitis scrofulosa by applying tuberculin to the skin is in favour of this view.

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Gold Dermatitis, treated with B.A.L. Toxic Manifestations ? Related to Calcium Deprivation.—BERNARD GREEN, M.R.C.S., L.R.C.P., and BRIAN F. RUSSELL, M.D.

T. W., male, aged 57.

First seen (B. G.) on October 29, 1947, showing a polymorphous eruption of urticarial, erythematous and exfoliative lesions all over the trunk, limbs, scalp, face and neck.

History.—He had suffered from rheumatoid arthritis for eighteen months, and at his local hospital had been given a course of myocrisin, one per week (total amount not known). About the seventh injection he noticed some irritation of his skin between the clefts of the fingers, but he did not mention this to his doctor. After the ninth injection he reported the irritation, which by this time had spread to the palms. The injections of gold were immediately stopped, but within a few days he developed a generalized eruption with intense irritation. He was given a course of eight injections of intravenous sodium thiosulphate. This helped the irritation and the eruption to some slight degree. He was then given a course of B.A.L., four injections in the first twenty-four hours, two on the second day, and one on the third day. (Total amount of B.A.L. not known.) After the second injection the "rheumatism" returned, particularly in his shoulders, and remained painful for twenty-four hours, then the right knee became affected, the leg being fixed in a flexed position; this remained so for twenty-four hours, when the left knee became similarly affected. He also had a "cramp" of the left hand and forearm lasting one to two minutes; this occurred about four times at various intervals of time. In addition, he had attacks of excessive sweating every night after the injection of B.A.L. whilst in hospital, and a number of shivering attacks—on one occasion he was unable to feed himself and had to be spoon-fed.

He was considered sufficiently recovered from the gold dermatitis, and was discharged from the local hospital about October 15, 1947.

Two weeks later (October 29) he consulted me (B. G.) as a private patient. He was then suffering from a relapse of the gold dermatitis, with lesions as stated above. It was during the time of my examination he developed a tonic muscular contraction of the flexor muscles of his left forearm and hand, which disappeared within a few minutes following massage, and in addition he had a shivering attack.

I had him admitted to St. Bartholomew's Hospital, and ordered a course of B.A.L. to be commenced immediately. The improvement was dramatic, and within a few days he had considerably improved. Whilst in St. Bartholomew's Hospital he had no shivering attacks and no visible contractions of his muscles, but he complained of pain in the right shoulder lasting about two days. He was discharged on November 12, having sufficiently recovered to warrant out-patient treatment.

A series of blood calcium level estimations have been carried out (see Dr. Brian Russell's comment). Chvostek's sign was found to be positive.

Seen on November 17, 1947, when the patient complained of slight irritation all over the body. Examination revealed some fine scaling of the face, scalp, forearms and legs; erythema of scrotum and generalized pigmentation.

Comment (B. G.).—This case demonstrates the possible toxic effects of B.A.L. and its relation to calcium deprivation of the tissues. The points of interest are the pain in the shoulder and knees—with fixation in position of flexion—the tonic contractions of the flexor muscles of the left hand, the shivering, sweating attacks, and the presence of the Chvostek's sign after the injection of B.A.L.

Comment (Dr. Brian Russell).—The occurrence of cramp-like pains in the limbs and carpal spasms in this patient suggested a state of latent tetany, and this was confirmed by the presence of Chvostek's sign. The absence of alkalosis made it probable that the tetany was of low calcium or magnesium type.

Subsequent studies after a test dose of 2.41 mg. B.A.L. per kg. repeated in one and a half hours resulted in the following observations: a rise was noted in systolic and diastolic blood-pressure to a maximum increase of 19 mm.Hg and 24 mm.Hg respectively two and three-quarter hours after the first injection. Diastolic readings were obtained with difficulty at this time, particularly the second and third of each group of three readings. At the same time difficulty was experienced in the withdrawal of samples of venous blood and of inserting the needle in the vein. These difficulties were thought to be due to vascular spasm, particularly as spasm was also noted with galvanism in attempting a quantitative record of Erb's test. This was preceded by a sharp reduction in muscle sensitivity to galvanism, contrary to the expected changes from tetany but at least evidence of a profound disturbance in kationic equilibrium.

Changes considered significant and maximal half an hour after the injections were noted in the serum calcium level.

Nine volunteers and patients have been injected with doses of B.A.L. between 0.75 and 3.34 mg. per kg., and Chvostek's sign became positive in five of these half an hour after the injection, including the recipient of the smallest dose. Of the remainder, one vomited and had cramp, a second had nausea and cramp, the third had cramp, and the fourth was entirely free from symptoms. This was a patient suffering from an acute and severe gold dermatitis, the only one in the series.

Three controls injected with 5% benzyl benzoate in arachis oil in volumes equivalent to those used for administering 1.31 to 2.89 mg. of B.A.L. per kg. had no symptoms or abnormal signs.

A tenth individual injected with 5.71 mg. of B.A.L. per kg. had a positive Trousseau's sign in addition to a positive Chvostek's sign one hour after the injection, and also complained of cramping pains in the chest, abdomen, shoulders, knees, calves and toes, with stabbing pains in the eyes, tickling, constricting sensations in the throat, and pains in front of the ears.

In addition to changes in the serum calcium level, significant changes in serum inorganic phosphorus (25%) and serum magnesium (65%) have been noted in the only patient so studied up to the present, but the serum potassium and serum sodium have not shown appreciable changes.

Finally it is noted that the symptoms of toxicity from B.A.L. described by Sulzberger *et al.* (1946) and Modell *et al.* (1946) can all be explained as tetany. Further, Durlacher *et al.* (1946) in animal studies describe a metabolic acidosis attributed chiefly to an accumulation of serum lactic acid and resulting in a reduction in the

pH of the blood and in the plasma CO_2 content, so that the tetany cannot be due to alkalosis and can only be produced by disturbances in pericellular kationic equilibrium probably from depletion or unavailability of calcium or magnesium or both.

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Other cases were shown as follows:

? **Lentigo Malignum**.—Dr. HUGH GORDON.

Herpetiform Dermatitis associated with Gaisboeck's Disease.—Dr. H. W. ALLEN.

(1) Multiple Sebaceous Cysts of the Vulva. (2) Severe Acne Necrotica of the Face.—
Dr. BEATRICE LEWIS.

(1) Porokeratosis (Mibelli); (2) Tuberculosis Cutis.—Dr. ALAN LYELL (for Dr. C. H. WHITTLE).

Case for Diagnosis: Pyodermia of Legs.—Dr. I. MARTIN SCOTT.

Multiple Benign Sarcoid (Boeck).—Dr. E. COLIN JONES.

(These cases may be published later in the *British Journal of Dermatology*.)

Section of Surgery

President—Sir MAX PAGE, K.B.E., C.B., D.S.O., M.S.

[November 5, 1947]

Surgical Records

PRESIDENT'S ADDRESS

By Sir MAX PAGE, K.B.E., C.B., D.S.O., M.S., F.R.C.S.

THE title of my Address is perhaps somewhat ambiguous. I may say at once that I do not propose to enlarge upon the high spots of surgical achievement but rather to consider some of the shortcomings of our craft, particularly shortcomings in the keeping of case records and in their application to scientific judgment.

We all seek the truth and endeavour to make wise use of it when it is found; but truth is as elusive in relation to our art as it is in any other branch of science, in particular the barrier to the establishment of satisfactory controls is often insurmountable. Moreover the discipline of science is not natural to man; it seems to come easily to a few but most of us find it a hard taskmaster. New ideas and new methods in surgery are forever coming before us and our task is to use our judgment unworried by impressionism and prejudice.

Looking back on British surgery of the last fifty years one cannot but feel that there was often failure in this respect. These weaknesses are familiar to most of us but I think it may be useful to pass them in review in support of my theme—better records and their more scientific use.

The progress which has been registered in surgery during the past half-century has been so great and has been so generally acclaimed that it seems almost churlish to emphasize the stumblings and backslidings which may be observed in this progression; however, the history of the development of any art is well worth study and may properly furnish later generations with a guide or a warning.

The first half of this century is certainly unique in the history of surgery. From its commencement we were endowed by the pioneer work of Lister, Roentgen and others, with knowledge and methods which, when fully developed, provided a hitherto unexampled precision in diagnosis and safe access to all parts of the body. It is noticeable that early enthusiasm begotten of this new freedom was directed mainly into the field of abdominal surgery and the locomotor system was relatively neglected.

The surgeons of the first decade were naturally influenced by the social atmosphere of their time as well as by the current scientific training. The spirit of Victorian individualism and privilege was manifest in their professional work. Jealousy of colleagues and fear of competition of juniors was too often an impediment to co-operative work. The ambition for personal success, ever a potent incentive to mankind, was often directed to the building up of their private practice, the advancement of surgical knowledge tending to take a secondary place. So far as institutional facilities are considered it may be recalled that in the first quarter of this century London possessed no organized centre for the study of surgery comparable with the Mayo Clinic, the surgical centres of Boston and Baltimore or some of the professorial units on the Continent. Add to this the rigorous and insistent demand that dogs the surgeon for the immediate relief of the sick and it will not appear surprising that with this background scientific judgment of new operations was slow to make itself felt. Of this lag I will now quote some specific examples. Operations for acute appendicitis only came into vogue after Treves had operated on Edward VII in 1902, but once the inflamed appendix was recognized as lawful game for the surgeon, the call for operative treatment at any stage of an attack was soon regarded almost as a law. Indeed it must be remembered that this doctrine was maintained by many surgeons until quite recently. To us it may seem fantastic to break in on an infected intraperitoneal organ which the natural processes have manifestly localized, but the surgeons of thirty years ago were still mechanically minded and gave little credit

to Nature's defence methods. It is true that there were exceptions to this radical attitude: Ochsner, in his book on Appendicitis, published in 1906 made out a strong case for non-operative treatment under certain circumstances. Sperren, who had found in 1905 that the mortality after operations for acute appendicitis at the London Hospital was 19.5%, was inclined to conform with Ochsner's views. However, the lack of convincing records of cases dealt with conservatively as advocated by Ochsner, Sherren and others, and the absence of an analysis of the results of intemperate intervention, were no doubt partly responsible for the persistence of a fixed idea. That we are still not fully informed as to the morbidity and mortality of appendicitis is suggested by some statistics, extracted from the Registrar-General's Report, and put forward by Dr. W. T. Russell at Oxford last summer. They have not yet been published and further work in relation to them is afoot, but here is the main statement:—

THE STANDARDIZED MORTALITY RATIOS FOR APPENDICITIS AT AGES 20 TO 65
FOR MALES DURING THE PERIOD 1930-32 IN ENGLAND AND WALES

Social class	Males			
I	181
II	140
III	98
IV	80
V	76

The standardized mortality ratio is the percentage ratio of the deaths actually registered to the "standard deaths". The "standard deaths" are those which would occur if the population at specific ages in a Social Group died according to the corresponding death-rates for all males in those age-groups.

Why the mortality in the professional and executive classes should be more than double that of manual workers is an interesting conundrum and I will forbear from speculating on it. One hopes that in the near future more light will be thrown on a matter of such close interest to surgeons.

Turning to gastric surgery, the most striking feature was the prolonged popularity of some type of short-circuit operation for pyloric and duodenal ulcer. The want of knowledge of the frequent failures of this procedure when it had been applied to stomachs without obstruction and with a high acid must be attributed to a defective follow-up. The side issues of partial gastrectomy are being brought home to us with a rapidity which is almost disconcerting. No doubt it is possible in this relationship that the evil results may be found to be relatively uncommon when a balanced view is forthcoming after a careful statistical study.

One of the odd vagaries of the surgical generation under review was the craze for various "pexies". This type of operation was first popularized on the kidney; the fashion subsequently extended to the large bowel and the stomach. It may be agreed that fixation of the kidney is justified in certain rare instances of intermittent hydronephrosis; its wholesale adoption as a cure for vague abdominal complaints was, I think, due to a failure to appreciate how often considerable mobility of the organ is present without giving rise to any symptoms. The attempts to fix the hollow viscera, in what was regarded as their proper position, were no doubt due to the reaction of a mechanically minded surgeon to the new evidence brought forward by the novel radiographs of barium shadows. If the position of the bowel so shown did not conform to the current conception of textbook anatomy, then this supposed malposition was held responsible for almost any abdominal complaint. Operative replacement and fixation were felt to be reasonable remedy.

Whatever value these operations may occasionally have possessed for mechanical reasons, and though they did little immediate harm, it is now generally agreed that they fall into the category of irrational surgery. The basic cause of the complaint remained unrecognized and the operation was little better than a surgical nostrum.

The patients who submitted to this type of procedure belong to a group who will ever be treated in accordance with the prevailing fashion in medicine. Nowadays we generally attribute their troubles to psychological causes or to some upset in the endocrine balance. At any rate we withhold the knife as long as possible.

Another peculiar surgical myth was created by that brilliant surgeon, Arbuthnot Lane, to whom surgery owes a full appreciation of the meaning of asepsis. His conception of the role of intestinal stasis in man led him to advocate at first short-circuiting procedures, and, subsequently, extensive colectomy for conditions as far separate as chronic mastitis and toxic goitre. I do not think his practice was widely followed in the profession but this development forms an interesting example of how far a strong and imaginative personality can lead surgical judgment into mythical fields when unfettered by scientific control.

A more definite example of the lack of guidance from proper records is to be observed in the assessment of the value of hernia operations. For thirty years or more after Bassini's method and its various modifications had been widely accepted, almost any surgeon, in his publications or in conversation, would express the opinion that there was hardly any recurrence after his own operations. Yet an independent investigation of some 300 cases undertaken in 1934 by Barrett and myself showed that the recurrence rate for inguinal hernia occurring in the Metropolitan Police was over 20%. I must admit that our figures were not exposed to statistical criticism of the expert class, but similar results have since been published by other observers. It cannot be said that the operative cure of hernia is yet established on an agreed basis, but the figures referred to have drawn attention to some of our failures and have provoked a closer consideration of technique and stimulated the establishment of better follow-up systems.

In connexion with the surgery of the breast there are some outstanding problems which one might think should have been settled ere now on a statistical basis. The views we adopt in this field have most serious repercussions on the well-being of the patient and have excited interest among surgeons for many years. I refer first to the theory that cystic disease in a breast predisposes to the development of carcinoma; clinical experience of many, and some animal experimental work, does not favour this view, but the crucial proof by figures does not seem to be available. Secondly, some surgeons are still in doubt as to the necessity for a full radical amputation in all instances of carcinoma of the breast.

In the field of fracture work satisfactory statistical guidance, both on general principles and in relation to the management of individual fractures, had to wait for the establishment of organized fracture clinics of which Sir Harry Platt was the protagonist in this country. I think that the major problems of delay, or failure in union, are not yet conclusively solved. This may well be attributed to the absence of a true statistical picture of the incidence of these conditions in relation to the various methods of treatment.

So far I have quoted examples from what is called general surgical practice. In the field of the major specialties, genito-urinary, neurosurgical and thoracic, I am ill-placed to be critical, and in general I can but applaud the level of achievement in these groups. I think that there is little doubt that those who specialize have maintained a high standard of case records with emphasis on careful follow-up methods. This statement also applies to most of us in relation to our own major interest—and few of us are not specialists in some measure nowadays. One may deplore the gradual extinction of the general surgeon, but one has to face the fact that the spear-head of surgical advance rests now in the hands of the specialist. The general surgeon will, of necessity, survive in isolated areas and in the Services, but how he is to be replaced in our educational system is a difficult question to answer. We shall always need some authority to synthesize the elements of surgical advance, an authority that can present a broad view of the surgical scene for the benefit of new recruits. Perhaps the mantle will fall on the broad shoulders of the whole-time professors.

Returning to my thesis I think I have shown that in the course of its rapid development modern surgery has been over-dependent on judgments tinctured by the emotional reactions common to mankind, and that it has largely failed to utilize statistical research. No doubt each generation of scientific men tends to

emancipate itself further from its intellectual inheritance and the present one is in need of no incentive in this direction from me. To have all surgeons fully trained as scientists is neither possible nor perhaps desirable, but it certainly behoves us so to plan our work that wherever possible scientific statistical control may be facilitated. I would submit that we should give greater attention to our records and systems of follow-up which must form the basis of any such study.

Case records have a dual purpose, the individual and the general. The purpose of the first is to conserve and provide medical information about the patient in his future interest. To this end the inclusion of accurate information from all departments under one cover, so indexed as to be easily obtainable, is obviously desirable. The second purpose is to provide the material which will facilitate the collation and comparison of varying forms of treatment. They are the bricks without which the statistician cannot build. It is in this latter respect that we are faced with the difficulty of selecting or omitting facts. We are all familiar with the difficulties met with when an investigation is undertaken which involves abstracting notes from several institutions; too often one is baulked by the absence in many records of some crucial information. This is a difficult matter to remedy and one is forced to the conclusion that most organized study requiring statistical information must be planned ahead, an agreed pro forma being circulated among those taking part in the investigation.

It is evident that since the first World War there has been a considerable advance in the keeping of surgical records. Individual surgeons and institutions have led the way. I think the establishment of wholtime surgical units has been a powerful influence assisting this change.

It may be said that surgical judgment must depend mainly on pathological knowledge and clinical judgment, none the less there are certainly many questions that can only be answered by statistical investigation and there is at present a strong movement in favour of a more scientific use of that method.

In the sphere of public health and social medicine the essential need for the work of a statistician is fully recognized. I have not enough knowledge to know how far he can assist the surgeon but I think his help should clear up many problems which have for long baulked us. I trust we shall maintain a critical, but open mind towards any new surgical experiment, and while welcoming help from any source which may assist the advancement of the standard of our art we need not be mesmerized into the acquiescent reception of all records stamped with a statistical hall-mark.

Mr. H. Cotton said that planning for health in all manner of ways was a very topical subject. The essential precedent to successful planning was a full knowledge of the facts, and then not as isolated facts, but in relation to one another. The lack of related knowledge was marked in the field of health and sickness. Mortality statistics, which had been available for over one hundred years, did not reflect the sickness situation, nor did they indicate the range or the success of surgical procedures. His theme for that evening was that surgery did not do itself justice. The true greatness of surgical achievement was concealed, due to the lack of simple records made at the time and on the spot by the only persons able to make them authoritatively. From the aggregation of such reliable records much could be made to emerge. Statistics, whether elementary or recondite, could never be better than the records from which they were compiled. He had to confess that when he examined hospital records he was chiefly impressed by the amount of information which was lacking. There were frequently the most gross omissions in a patient's notes, many of which were so sparse as to be of no real value. While oral instruction and visual demonstration were still the best methods of instruction, there had been such a growth in the range of knowledge that these could not be given to everybody on every subject. Therefore there had to be more reliance on published and unpublished records, whether in the form of books or individual case notes. Where these were defective, seekers after knowledge were deprived of necessary instruction.

But the prime function of the record was that of assisting the surgeon in the treatment of his patient. He would define a medical record as a collection of authenticated observations, opinions, reminders, and instructions. It was a scientific instrument if it presented accurately, in a form comprehensible to others, the facts observed, the procedures undertaken, the reaction to these procedures, the results of tests, the narrative of progress, and the long-term results of all of the work carried out. With such a scientific instrument, wherein the various measurements, assessments, reliefs and results of the patient's illness or injury were rationally arranged, easy to read and capable of summation where large numbers of cases presented broadly similar characteristics, the surgeon had, he suggested, an instrument of no less worth than certain of the weapons in his theatre armoury.

The statistical data provided by the hospitals of this country, and even of America, were singularly lacking in even gross details of information, although some institutions and clinics did furnish particulars of their own work. But such refined statistics were not of the value they could be were they placed against the broad background of gross figures. Nor was there a satisfactory common code of nomenclature of the various surgical practices and procedures.

He thought that the development of surgical recording should proceed in stages. The surgeon's time had to be conserved; all that should be expected of him was that he should say what each record should contain concerning his own work.

Thus there was a necessity for pre-arrangement, as follows :

- (1) Prior agreement on what are operative procedures and what are not.
- (2) Agreement as to which operative procedures are to be recorded and which are not.
- (3) There must be an accepted terminology of operations.
- (4) Agreement on the point in time at which the end-result of a given type of operation is assessed.
- (5) Every convenience must be provided for the surgeon to contribute to the record without interfering with his main job.

In regard to the first it was possible to define an operation if one accepted certain basic groups, as had been suggested by the American Medical Association in their publication entitled "The Standard Nomenclature of Disease and Operations". Fundamental surgical procedures were there divided into nine groups, namely: incision, excision, amputation, introduction, endoscopy, repair, destruction, suture and manipulation.

There was an infinity of variants in operative procedures as well as in complaints, so that, unless some guiding principles were laid down, the data might defy compilation. With regard to operative terminology the ground was particularly difficult, since there was a lack even of nationally accepted nomenclature of operations. This made the work of any lay statistician very difficult indeed. The curse of the non-surgeon in dealing with surgical terminology was the eponym, and a descriptive term should here be added for the benefit of the inexpert.

Another difficult point arose in statistics of the end-results of operation. The day-to-day preoccupation of surgeons did not allow of comprehensive follow-up departments. But if follow-up and final assessments were prescribed for only 12 or 20 of the commonest operations, some basis of comparability could be achieved.

He turned now to what the surgeons were entitled to expect in return for all this. There was a necessity for some type of pro formas and questionnaires in which the physician or surgeon was asked to fill up only that part which could not be filled up by anyone else. The first need was for a standard operation report, not complicated by headings for all sorts of rare occurrences, but covering the simple facts of what was found and what was done. From this there could be compiled an operation census, which must precede any refined statistics. For the surgeon interested in the particular operation there was no difficulty in designing a form of report from which even the most esoteric statistics could be compiled. It was essential that operation

reports should be made immediately the operation was over. It was sufficient if the surgeon barked out a swift summary of his discoveries and his actions to some assistant who had the necessary tablets on which to set them down. There was also the method of using a dictating machine.

The operation record was, of course, no more than a part of the general record of the patient during his stay in hospital; many other contributors furnished material to the complete record, which was an instrument in the hands of a clinician, a synthesis of everybody's findings. It was also an educational, research, planning and administrative instrument.

An outstanding need to-day was for a broadly uniform system of medical record-keeping in British hospitals. His conception of a uniform system did not mean regimentation. But it meant that all hospitals should follow a few well-defined, easily comprehended principles, and that individual hospitals should make such adjustments as they desired. From this it followed that there was a need for persons versed in the plan and skilled in the technique of medical record-keeping.

[December 3, 1947]

DISCUSSION: THE TREATMENT OF CANCER OF THE BREAST. [Abridged]

Sir Gordon Gordon-Taylor, after outlining the age-long history of cancer of the breast, continued: Time is lacking to recount the whole story of the evolution of what till a few years ago might have been veritably termed radical mastectomy performed in the "proper cancer spirit", and I would refer those interested to the learned papers of William A. Cooper of New York and our own lamented Sir D'Arcy Power. The descriptions of many of these pristine operations are reminiscent of the martyrdom of the saints, while the barbarous armamentarium of men like Scultetus, Fabricius Hildanus, Bidloo or Tabor to facilitate the removal of a breast recalls the crude methods and cutlery of *les sales Boches* within more recent times.

The spirit of chauvinism still burns within me, and I gladly pay my humble tribute to those from the Middlesex Hospital who have contributed to the evolution of the radical operation, especially Charles Moore, whose epoch-making paper appeared in 1867, my old surgical teacher Sir Alfred Pearce Gould, whose private assistant I was for nearly ten years, and my distinguished colleague and firm friend, W. Sampson Handley. In 1903, as a fellow-worker in our Cancer Research Laboratories at "Middlesex", I saw the inception of the pathological work which has made Handley world-famous, and the operation which he designed in those far-off days to meet pathological requirements has been that on which I have largely modelled my own surgery of mammary cancer.

I may not have followed Handley in his employment of radium at the time of operation or in the use of post-operative radiation, but have always allowed my own enthusiasm the fullest scope and have more than a dozen times deliberately removed the chain of anterior mediastinal glands along with the internal mammary vessels after resection of the second and third costal cartilages. Now, in retrospect, I rather regret that I have not availed myself of this added step towards the truly radical on many more occasions: my end-results might have been bettered thereby.

Other important contributions germane to this discussion have emanated in more recent times from my own hospital and are deserving of attention: those of Patey, Scarff and R. S. Handley on the histological grading of mammary tumours and its prognostic importance; Brian Truscott's recent and most valuable paper on a "follow-up" of 1,211 cases of mammary carcinoma treated *omni modo* in "Middlesex" from 1926 to 1940; and Thackray and R. S. Handley—distinguished son of a famous father—who have investigated the anterior mediastinal glands in a series of cases of breast cancer.

The varying fashion in the treatment of cancer of the breast might be termed "the wax and wane" of radical mastectomy. For be assured, when once the ancillary methods of surgery are added to the knife in dealing with cancer the extent of the operative removal irresistibly, inevitably becomes curtailed: nor is it otherwise in the treatment of mammary malignant disease. Confidence in pre-operative and post-operative irradiation has for some years indubitably tended to restrict the extent of surgical ablation; curtailment of operation is noted especially in the amount of skin and muscle removed and the clearance of the axilla. By some radium has even been regarded as the equal, if not the superior, of radical surgical removal.

In order to secure some information as to the practice of other surgeons in respect of supplementary radiation, in 1938 I approached 72 of my surgical friends throughout the length and breadth of Great Britain. Four different usages apparently prevailed a decade ago; of the surgeons interrogated 25% made no use of irradiation as a supplement to radical operation; 44% employed some form of irradiation as a supplement to every radical operation; 29% used it only after radical operation in Stage II cases; 2% favoured irradiation with or without a local operation.

How has the employment of ancillary radiation fared since 1938? The distraction of surgical attention towards other problems, especially trauma, during the war years and the absence abroad of many operators of first rank necessarily thrust much of the treatment of cancer on to hard-pressed but ever-willing radiotherapeutic clinics, perhaps especially in those parts of the country which were fortunately spared the ravages and disorderings of war. Unfortunately recommendations are nowadays finding their way into the literature which, so far as the incompleteness of radical mastectomy is concerned, take us back to the procedures of Scultetus and others of the Dark and Middle Ages.

I am not, and have never been a "cancer specialist"; I have never had a cancer clinic or sat among the mighty in Cancer Campaigns. I am a simple soul, a simple surgeon profoundly ignorant of the recondite mysteries of radiation therapy, and very fearful of the wondrous apparatus under the management of these scientific experts. But I would hasten to disabuse you of any thought that I harbour even the very faintest suspicion of antagonism towards my radiotherapeutic confrères, least of all towards my friend and colleague Brian Windeyer, who has so often brought aid to myself and healing and comfort to my patients. I yield to none in my admiration for those who practise the radiotherapeutic art, realizing full well the constant demands on their sympathy and cheerfulness, full of wondering amazement at their devotion in a type of work which may well undermine their own health and may often nigh break their spirit. In respect of the advanced inoperable cases my debt to these men is incalculable, and it is for this advanced class of case or for patients deemed unsuitable for radical surgery on other grounds than the stage of the malady that I reserve X-ray therapy. Save for one very brief and perhaps fortuitously unhappy period long ago I have personally eschewed the method of post-operative radiation as a supplement to radical surgery in the cases of mammary carcinoma which are by common usage now classified as Stage I and Stage II. For such I have preferred a sharp knife, a stout heart and unquenchable optimism, and have regarded the widest radical surgery untrammelled by ancillary radiation as the method of election in almost every case belonging to these two categories.

Few of the papers dealing with radiation have made any reference to the *morbidity from radiation therapy*: apart from unhappy local effects, the sickness, misery and other untoward sequelæ may lower the patient's resistance to any malignant cells that may remain after surgical operation.

Cancer resistance or immunity.—It is amazing how the disease may return many years after operation, at a time when the original malady has been almost forgotten. Truscott in 1947 from his investigation reiterates the statement of Mitchell Banks in 1900 that no matter how early the case or thorough the treatment, no patient is free from the possibility of recurrence until death occurs from some other cause.

Recurrence has certainly taken place as long as thirty-two years after the initial operation; Frank Steward recorded a thirty-one-year recurrence in a woman operated on originally by Butlin; Bryant relates recurrences at thirty-two, thirty-one and twenty-five years. Verneuil operated on a recurrence thirty years after the first operation; Bowlby on a case dealt with by Sir Thomas Smith twenty-four years previously.

I have myself seen a carcinoma of the breast recur in the pelvis as a mass, the histological structure of which was reported as a "spheroidal-cell carcinoma of mammary type": the breast had been radically removed by Sir Cuthbert Wallace thirty years before. Three cases of recurrence in the scar of a radical mastectomy were observed by me twenty-one, twenty-two and twenty-three years after operations by other surgeons.

In some cases no causal factor except perhaps *age* can be impugned as bearing any relationship to the recrudescence of the malady, but in others recurrence does appear to have been *preceded by intercurrent disease, or by surgical operation for some independent condition*. In one patient of my own a recurrence in the scar developed seventeen years after a radical mastectomy, and a few weeks after a very severe attack of acute pyelonephritis. I have also observed recurrence in the scar following an operation for hæmorrhoids performed sixteen years after the initial amputation. In three cases recurrence followed shortly after a gall-stone operation, and in another patient recurrence seemed to be related to a herniorrhaphy performed under local anæsthesia! In such cases what Sir Alfred Pearce Gould in his Bradshaw Lecture termed "cancer immunity" appears to have been broken down by happenings unconnected with the original disease.

The vagaries and variations of this cancer immunity or resistance are to be occasionally seen in the recurring alternation of efflorescence and retrogression or disappearance of cutaneous nodules and even of lymphatic glands. Preternaturally slow growth of a mammary tumour and the prolonged absence of metastases may be indicative of the same cancer resistance; the most remarkable example is that of Crivelli and Tinca, whose patient had a carcinoma of the breast for forty-seven years, and only in the last two years of her life did the disease obtain the mastery.

Still more amazing are the cases of *spontaneous disappearance of a cancerous mammary growth and its secondaries*. Sir Alfred Pearce Gould in his Bradshaw Lecture quoted a number of his own cases in which this phenomenon occurred, even when the patient had been almost *in articulo mortis*. Not a few of the cases mentioned by my old "chief" were personally known to myself, but I doubt not that many of the older surgeons here have been privileged to see such miracles. "Cancer, even when advanced in degree and of long duration, may get better, and does sometimes get well. Nature unaided may sometimes effect a cure." These statements are based on fact: I have not the wit or wisdom to weave them into theories, but I remain fearful of any form of treatment or contingency which may even temporarily undermine the patient's resisting power to deal with residual malignant cells that may have been left behind at operation. Some of my patients with an axilla packed with infected glands, in whom it seems impossible that every cancer cell can have been removed, have remained well for periods of fifteen to twenty years, in the absence of post-operative X-ray therapy.

Forty years have passed since I performed my first radical mastectomy, and although I have been attached synchronously to a plethora of hospitals, I confess to my surprise in June 1938 to find that I had performed 603 radical operations for carcinoma mammæ. The year that intervened between the Plymouth meeting of the British Medical Association in 1938 and the outbreak of hostilities added another 25, but the war years where my function was that of a consultant rather than an operating surgeon and those of more recent wanderings have only yielded an additional 17 radical ablations. My operative experience therefore amounts to 645 radical operations for mammary cancer, while less than one hundred patients have for various reasons been treated by radiation only, a very few by limited operation

and radiation or left without any active therapy. The ten-year figures which follow¹ are the story of one surgeon's experience, which on the whole has dealt with what might be regarded as a relatively favourable class of case.

Total personal cases of primary carcinoma of the breast, from December 1907 to December 1947 treated by radical operation, radiation alone, removal of the breast and superadded irradiation or no therapy: under 750.

Total cases of primary cancer of the breast dealt with by radical operation from December 1907 to December 1947	645
Total cases of primary carcinoma of breast submitted to radical mastectomy up to June 1938	603
Cases of radical mastectomy from June 1938 to September 3, 1939	25
Cases from September 1939 to December 1947	17
Total	645

Lazarus-Barlow and Campiche, in a statistical survey of 1,976 cases of mammary cancer from the Middlesex Hospital records up to 1904, estimated that the average *natural duration of the untreated disease* was 25.4 months in cases with a large amount of fibrous tissue and few cells, and five and a half years in the more cellular growths. *The average natural duration* of all cases was computed to be three and a half years—a figure with which Rowntree is in agreement. It would therefore be almost impertinent in this assembly of surgeons to discuss five-year results, and I will therefore confine my statistics to ten-year survival cases. It is refreshing to find Truscott in his recent paper considering the fate of patients ten years after treatment.

Total cases of radical mastectomy up to 1928, i.e. cases that could have survived ten years or more	363
Stage I: Cases operated up to 1928	113
Cases surviving ten years	95
Percentage surviving ten years	84.07
Stage II: Cases of radical mastectomy up to 1928	204
Cases surviving ten years	60
Percentage surviving ten years	29.4
Stage III: Cases operated up to 1928	46
Cases surviving ten years	3
Percentage surviving ten years	6.5

By August 1939, 169 (43%) of all my 388 patients in whom radical mastectomy had been performed up to 1929 had survived ten years, many being of course still alive at that time.

Survival between twenty-five and thirty years	8
Survival of twenty to twenty-five years	6
Survival of fifteen to twenty years	33
Survival of ten to fifteen years	122
Total	169

Where information is lacking as to the histological grading of the breast tumour, no two series of cases or of treatments can be fairly compared.—Far be it from me to vaunt the results of my own obstinate old-fashioned surgery or challenge my findings against those of other men and of other methods; almost without exception the conclusions of the surgeon-radiotherapist “combines” are based on a five-year survival basis, which is not a very ambitious yardstick, when the length of the natural history of mammary cancer is borne in mind. When their figures at ten years convincingly surpass those which I have given from radical surgery alone, I may be prepared to solicit the routine aid of radiotherapy for the Stage I and Stage II patients.

¹I have with some reluctance yielded to the suggestion that reference should be made to my own results at five years. The only real difference between the five and ten-year figures concerns the Stage II cases, of whom 40% are alive at five years, and 30% at ten years.

Among cases that have survived more than thirty years one of my patients with several infected glands in the axilla at the time of operation is alive thirty-seven years after; another was run over and killed in a Gloucestershire street accident thirty-six years after operation; a third died thirty-six years after the initial operation from what may have been an abdominal recurrence thirty-six years after; while a fourth is alive and well just over thirty-three years after removal of a carcinomatous breast.

Considerations of time preclude me from dealing with the details of operative technique, or to pay adequate tribute to George Grey Turner in respect of this as in every branch of surgery. There are no minutes left to consider the problem of pain, the œdematous arm, the occasionally dramatic effects of stilbœstrol, the value of sterilization by radiotherapy or the baleful results of pregnancy during the development of the tumour and the relation of any subsequent cysts to recurrence, &c. The patient with enlarged supraclavicular glands will live longer if treated by radiation therapy than by any operative attack. The most profound anatomist and skilful surgeon cannot perform a "block-dissection" of the supraclavicular fossa.

Dr. R. McWhirter: The method of treatment of breast carcinoma now in use in the Royal Infirmary in Edinburgh has been developed in an attempt to overcome the causes of failure of the radical operation. Unfortunately the extent of failure of the radical operation is too often concealed by presenting only the results obtained in highly selected cases. By selecting cases for the radical operation very carefully and by publishing the results only in the cases so selected the survival rates may be made to appear so good that the impression may be conveyed that there is little necessity to consider new and better methods of treatment.

It cannot be too strongly emphasized in the assessment of the value of a method of treatment that the value must be judged not simply on the results obtained when the method is applied but also by the number of cases to which it will apply. If a method can be applied to only a few selected cases it cannot be considered good just because the five-year survival rate is high in the few cases so treated. Cases considered to be beyond a method of treatment are just as much failures of that method as cases actually treated and failing to be cured.

When radical surgery is the only method of treatment available and when all cases coming (whether admitted or not) to a large general hospital are considered I do not believe the five-year survival rate will be found to be higher than 20% to 25%. Haagensen and Stout have shown that of all the cases of breast carcinoma coming to the Presbyterian Hospital in New York only 22.2% are alive at the end of five years. Similar figures are difficult to obtain in this country but Truscott (1947) has shown that of all operable cases (unfortunately he does not include inoperable cases) coming to the Middlesex Hospital in the period 1926 to 1935 only 28% are alive at the end of five years. These figures explain why the Registrar-General is able each year to record an increasing number of deaths from breast cancer. They also provide a better indication of the extent by which the radical operation fails.

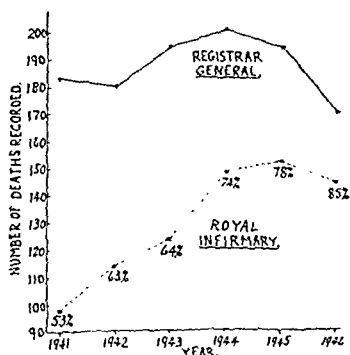


FIG. 1.—The number of breast-cancer deaths occurring in patients referred to the Royal Infirmary from the south-east of Scotland has been expressed as a percentage of the deaths recorded by the Registrar-General from the same area.

I believe the number of survivors should be expressed ideally as a percentage of the total cases occurring in the area served by the treatment centre. In Edinburgh we are approaching this ideal, because general practitioners in the area have been specially requested to send all cases, no matter how advanced, and fig. 1 shows that the number of deaths occurring amongst such patients referred to the Infirmary from the south-east of Scotland is approaching the number recorded by the Registrar-General in the south-east of Scotland. In 1946, 85% of the deaths recorded by the Registrar-General occurred in patients referred to the Royal Infirmary.

It will be noted that the two curves are rapidly converging and there is good reason to believe that almost all the cases of breast carcinoma occurring in the south-east of Scotland are now being referred to the Royal Infirmary. The results which will be presented from the treatment method in use in recent years are therefore based on figures showing a lesser degree of selection than any hitherto published. I am not aware of a similar position having been reached by any other centre, and it should be noted that this position was reached in Edinburgh only by requesting that all advanced cases

should be referred. When comparison is being made with the results obtained in other centres it must be appreciated that the survival rates in other centres will be based on a more selected group of cases.

Number of cases.—Since 1930 approximately 3,500 cases have been referred to the Royal Infirmary. For the purposes of this paper only cases from 1930 till 1945 will be included. During this period there were 2,809 cases and of this number 299 were referred only after failure of treatment elsewhere. When these recurrent cases are omitted there are 2,510 cases available for analysis.

TABLE I.—ALL PREVIOUSLY UNTREATED CASES—MANCHESTER CLASSIFICATION

		Stage I	Stage II	Stage III	Stage IV	Total
1930-34	..	138 35%	86 22%	133 34%	35 9%	392 100%
1935-40	..	267 34%	137 18%	157 20%	223 28%	784 100%
1941-45	..	405 30%	344 26%	182 14%	403 30%	1,334 100%
Total		810 32%	567 23%	472 19%	661 26%	2,510 100%

It will be noted from Table I that the number of cases in Stage IV is small in the period 1930-34, because advanced cases were not recorded.

In the period 1941-45 the number of advanced cases (Stage IV cases) is higher than in any other period.

Calculation of survival rates.—The method adopted is that advised by Dr. Lewis-Fanning of the Medical Research Council. It is of particular value in the calculation of the survival rate for the period 1941-45. A full account of the method cannot be given here but briefly it may be stated that, while the five-year survival rate of the cases treated in the period 1941-45 is mainly determined by the cases treated in 1941 the rate is also influenced by the cases treated in the later years. By allowing the more recently treated cases to influence the five-year survival rate a figure is obtained which is more reliable than that based on the 1941 cases alone.

Operability.—The cases have been divided into two groups "operable" and "inoperable". A low standard of "operability" has been accepted because in the earlier years many moderately advanced cases were actually treated by radical excision. It will be appreciated that if a higher standard had been accepted this would have resulted in higher survival rates amongst the "operable" cases. The following standard has been accepted and corresponds to Stages I, II and III of the clinical classification used in Manchester.

The primary tumour, which may be of any size, may show any degree of skin involvement up to and including ulceration but there must be no isolated skin nodules or other manifestation of invasion of the cutaneous lymphatics. The tumour may be fixed to the pectoral muscle but must not be fixed to the ribs. The axillary glands of the same side may be enlarged but they must not be fixed. The supraclavicular glands must not be enlarged and there must be no clinical or radiographic evidence of more distant metastases.

For reasons which will emerge later I believe it is inadvisable in such a definition to take into account the age or general health of the patient.

Untraced Cases.—The percentage untraced over the whole period is 0.24%. In the period 1941-45 only one case is untraced giving a percentage of 0.07%.

Histological examination.—Histological reports are available in almost every case where an operation was carried out and in the period 1941-45 97% of all "operable" cases are histologically proven, and of all the cases in this period 87% are histologically proven.

Methods of treatment used.—From 1930-34 the main method of treatment practised in Edinburgh was radical surgery alone and the cases in this period have been used as a control in the evaluation of other methods. From 1935-40 the main method of treatment was radical surgery followed by post-operative radiotherapy. From 1941-45 the main method of treatment was simple mastectomy followed by X-ray therapy.

The reasons leading to the changes which have been made will now be given.

RADICAL SURGERY ALONE: "OPERABLE" CASES

The causes of failure are so obvious when the radical surgical operation is attempted in "inoperable" cases that such a study is not profitable. But in the "operable" cases careful follow-up yields much valuable information and shows clearly that the operation often fails because of failure to eradicate all the disease in the operation area.

Of 364 "operable" cases treated by radical operation it was found that the number of cases developing recurrences in the chest wall, axilla and supraclavicular region of the side affected was almost 40% within five years of the time of the operation. Admittedly cells may have been present in distant sites as well but the finding showed that in 40% of cases the operation was doomed to failure because the disease was not eradicated locally.

TABLE II.—THE LOCAL RECURRENCE RATE IN 364 "OPERABLE" CASES TREATED BY RADICAL SURGERY ALONE

Years after treatment	Number of local recurrences	Number exposed to risk	Chance of developing local recurrence in any one year	Number developing local recurrences Total = 100
1	69	341.5	.202	20.2
2	20	232.5	.086	6.9
3	16	183.5	.087	6.4
4	8	148	.054	3.6
5	3	119	.025	1.6

The above figures are in general agreement with those published from other centres.

RADICAL SURGERY WITH POST-OPERATIVE RADIOTHERAPY—"OPERABLE" CASES

From this finding the first step was obvious and in 1935 it was decided to try the effect of post-operative radiotherapy to see if this procedure would be effective in destroying cells in the area of operation. The following table shows that it was effective and that the number of local recurrences has been reduced from 40% to 14%.

TABLE III.—THE LOCAL RECURRENCE RATE IN 278 "OPERABLE" CASES TREATED BY RADICAL SURGERY AND POST-OPERATIVE RADIOTHERAPY

Years after treatment	Number of local recurrences	Number exposed to risk	Chance of developing local recurrence in any one year	Number developing local recurrences Total = 100
1	9	271	.033	3.3
2	13	220.5	.059	5.7
3	5	171.5	.029	2.7
4	2	129.5	.015	1.4
5	1	86	.012	1.0

As might be anticipated from the foregoing remarks the five-year survival rate was higher and it was found to be raised from 37% for radical surgery alone to 51% when radical surgery was followed by post-operative radiotherapy. These figures still leave much to be desired for it must be borne in mind that the survival rates presented refer only to cases actually treated and take no account of the many cases treated only palliatively or not treated at all. It is important to do everything possible to raise the five-year survival rate in breast carcinoma because of all types of malignant disease in women, the breast is the site affected in 25% of cases. The disease, too, often occurs in young patients and one in eleven of the patients in this series was under 40 years of age.

SIMPLE MASTECTOMY WITH POST-OPERATIVE RADIOTHERAPY

It must be noted that however successful the localized post-operative radiotherapy may be the patient will still not be cured if cells have escaped beyond the area treated by X-rays. Some cells may have escaped to distant sites before the operation was performed but the possibility must now be considered of cells escaping beyond the operation area either at the time of operation or before X-ray treatment could be applied.

Because the radical operation not uncommonly fails to get rid of all the tumour tissue in the operation area it follows that at the time of operation tissues actually invaded by tumour must often be divided. The trauma inflicted on those involved tissues must increase the natural tendency of malignant cells to disseminate to other sites. Should cells be disseminated to other sites before radiotherapy is applied the radiotherapy will not be effective in saving the life of the patient. In an attempt to overcome this difficulty it was decided to explore treatment by simple mastectomy followed by post-operative radiotherapy.

At the time of the simple mastectomy, cells may still be liberated from the operation area on the chest wall but it is unlikely that these cells will escape beyond the intact barrier of the axilla.

Healing of the wound takes place more quickly after simple mastectomy than after a radical operation. Radiotherapy can therefore be applied with less delay. The interval during which cells may escape to distant sites is thus reduced.

The results already published by Keynes further supported the adoption of this method. It will be recalled that Keynes advised radium implantation following the local removal of the primary tumour or simple mastectomy if the tumour was large. He strongly advised against dissection of the axilla. The results obtained were good and the only difference between the present method and that of Keynes is that X-rays are used in place of radium implantation. X-ray treatment was deliberately chosen for no matter how carefully an implant is carried out it is exceedingly difficult to irradiate a large area uniformly and of course, in the areas where the dosage is low, recurrence is likely to take place. With high voltage X-ray therapy this difficulty is largely overcome and a large area may be irradiated in an almost uniform manner.

At first it may seem wrong not to dissect the axilla especially in early cases. In these early cases the axilla may or may not be secondarily involved.

If the axilla is, in fact, not involved it must be admitted that the radical operation is unnecessary, for extension of the operation to the axilla can do no good if there are no malignant cells to be removed.

On the other hand if the axilla is secondarily involved, it will be generally admitted that the results from radical operation are poor. This is the one fact which stands out in every published series of figures, and if one believes that radiotherapy has any part to play in the treatment of breast cancer it is surely desirable to see what results may be obtained from treatment of the axilla by radiotherapy.

Treatment of breast carcinoma by simple mastectomy and X-ray therapy was commenced in 1941 and it soon became obvious that it was possible to apply this method of treatment to almost every case and certainly it could be applied to far more cases than was possible when the radical operation preceded X-ray therapy. In view of what has already been said on the assessment of the value of a method of treatment all cases in each main treatment period will be included in the tables whether the cases were treated by the main method or not, and, in fact, whether they had any treatment or not.

Post-operative deaths have not been excluded from any of the tables. Indeed it has been assumed that the post-operative mortality in those cases operated on outside the Royal Infirmary was the same as within the Infirmary and the deaths assumed to have taken place have been added to the tables.

"Operable" cases will be considered in the first place.

SURVIVAL RATES OF ALL "OPERABLE" CASES

In the period 1930-34 the main method of treatment was radical surgery alone. The number of "operable" cases in this period was 359 and the five-year survival rate is 35.6%.

TABLE IV.—SURVIVAL RATE OF ALL "OPERABLE" CASES IN THE PERIOD 1930-34. MAIN METHOD OF TREATMENT—RADICAL SURGERY ALONE. TOTAL CASES, 359.

Years after treatment	Number of cancer deaths	Number exposed to risk	Chance of dying in any one year	Survival rate
1	89	358	.249	75.1%
2	66	267.5	.247	56.6%
3	32	200.5	.160	47.5%
4	19	166	.114	42.1%
5	22	142	.155	35.6%

In the period 1935-40 there were 569 "operable" cases and the main method of treatment was radical surgery and post-operative radiotherapy. The five-year survival rate is 44%.

TABLE V.—SURVIVAL RATE OF ALL "OPERABLE" CASES IN THE PERIOD 1935-40. MAIN METHOD OF TREATMENT—RADICAL SURGERY AND POST-OPERATIVE RADIO-THERAPY. TOTAL CASES, 569.

Years after treatment	Number of cancer deaths	Number exposed to risk	Chance of dying in any one year	Survival rate
1	94	568.5	.165	83.5%
2	102	472.5	.216	65.5%
3	52	366	.142	56.2%
4	42	307.5	.137	48.5%
5	24	261	.092	44.0%

In the period 1941-45 there were 941 "operable" cases and the main method of treatment was simple mastectomy and post-operative radiotherapy. The five-year survival rate is 55.9%.

TABLE VI.—SURVIVAL RATE OF ALL "OPERABLE" CASES IN THE PERIOD 1941-45. MAIN METHOD OF TREATMENT—SIMPLE MASTECTOMY AND POST-OPERATIVE RADIO-THERAPY. TOTAL CASES, 941.

Years after treatment	Number of cancer deaths	Number exposed to risk	Chance of dying in any one year	Survival rate
1	75	941	.080	92.0%
2	76	668.5	.114	81.6%
3	57	440	.130	71.0%
4	31	230.5	.135	61.5%
5	8	88	.091	55.9%

It will be noted that the five-year survival rate for the period 1941-45 is higher than in the two preceding periods. Statistical examination shows that the differences are significant. The findings therefore suggest that by not dissecting the axilla the risk of dissemination of cells to distant sites is reduced.

This conclusion is supported by the results obtained in the "inoperable" cases.

SURVIVAL RATES IN "INOPERABLE" CASES IN EACH OF THE THREE PERIODS

It was not of course possible or advisable to treat all "inoperable" cases by the method adopted for each period, for many cases were too advanced for any form of treatment or required only palliative treatment. The survival rate in these cases is influenced only by the effect produced by treatment in those cases where the disease is to some extent localized, i.e. in patients with fixed axillary glands, supraclavicular glands or involvement of the cutaneous lymphatics over the breast but with no evidence of more distant spread.

In many of these cases with extensive localized involvement it will be generally agreed that the radical operation is not only an unsuitable method of treatment but, if attempted, will often hasten the death of the patient. Notwithstanding what has been said the presence of supraclavicular glands did not always deter the surgeon from performing a radical operation and occasionally even when the axillary glands were fixed, radical removal was attempted. The term "inoperable" has, however, been retained as it would still appear to be appropriate for all cases in this category.

Simple mastectomy on the other hand may still be applied to cases where the glands in the axilla are fixed and where there are supraclavicular glands present and, as will be shown later, this treatment in association with radiotherapy may be practised with a considerable measure of success. It will be noted therefore that the term "inoperable" is used to denote a case beyond treatment by radical operation but not necessarily beyond other forms of treatment.

Again as this investigation is concerned with the true value of each method of treatment and not merely with the results obtained in treated cases, all "inoperable" cases, however treated, or even not treated, in each of the three main periods will be considered.

In the period 1930-34 few "inoperable" cases were recorded and none survived to the fifth year.

TABLE VII.—SURVIVAL RATE OF ALL "INOPERABLE" CASES IN THE PERIOD 1930-34. MAIN METHOD OF TREATMENT—RADICAL SURGERY ALONE. TOTAL CASES, 33

Years after treatment	Number of cancer deaths	Number exposed to risk	Chance of dying in any one year	Survival rate
1	22	33	.667	33.3%
2	6	10.5	.571	14.3%
3	3	4	.750	3.6%
4	1	1	1.000	0.0%
5	0	0	—	0.0%

In the period 1935-40 the number of "inoperable" cases referred was 221 and at the end of five years only 2.5% were alive. The results are little different from those obtained during the period 1930-34 and suggest that where a radical removal was attempted the post-operative radiotherapy was rendered ineffective by dissemination of cells at the time of operation.

TABLE VIII.—SURVIVAL RATE OF ALL "INOPERABLE" CASES IN THE PERIOD 1935-40. MAIN METHOD OF TREATMENT—RADICAL SURGERY AND POST-OPERATIVE RADIOTHERAPY. TOTAL CASES, 221

Years after treatment	Number of cancer deaths	Number exposed to risk	Chance of dying in any one year	Survival rate
1	138	221	.624	37.6%
2	54	83	.651	13.1%
3	13	29	.448	7.2%
4	9	15.5	.581	3.0%
5	1	6	.167	2.5%

In the period 1941-45 the number of "inoperable" cases was 404 and the five-year survival rate was 14.1%.

TABLE IX.—SURVIVAL RATE OF ALL "INOPERABLE" CASES IN THE PERIOD 1941-45. MAIN METHOD OF TREATMENT—SIMPLE MASTECTOMY AND POST-OPERATIVE RADIOTHERAPY. TOTAL CASES, 404

Years after treatment	Number of cancer deaths	Number exposed to risk	Chance of dying in any one year	Survival rate
1	186	404	.460	54.0%
2	83	182	.456	29.4%
3	25	69.5	.360	18.8%
4	4	26	.154	15.9%
5	1	9	.111	14.1%

Again the survival rates are higher than any obtained before and the differences are statistically significant when comparison is made with either of the two preceding periods.

In 205 (51%) of the "inoperable" cases seen during the period 1941-45 the disease was apparently still localized, whereas in the remaining 199 (49%) there was clear clinical or radiographic evidence of distant metastases. When the localized "inoperable" cases (see page 126) are considered alone, the five-year survival rate is 24.6%, and this figure shows still more clearly the advantages of the method of treatment advocated; as already shown when radical surgery alone, or combined with radiotherapy, were the methods of treatment in use, none or only a few cases survived to five years.

ALL "OPERABLE" AND "INOPERABLE" CASES OF CARCINOMA OF THE BREAST

This analysis would not be complete without consideration of the results of all cases, both "operable" and "inoperable". Unfortunately during the period 1930-34 no records were kept of patients admitted to medical wards, and of patients who were never admitted. Accordingly comparison can only be made between the two periods 1935-40 and 1941-45.

In the period 1935-40 the total number of cases, "operable" and "inoperable", referred to the Royal Infirmary was 790 and the five-year survival rate was 32.4%.

TABLE X.—SURVIVAL RATE OF ALL "OPERABLE" AND "INOPERABLE" CASES IN THE PERIOD 1935-40. MAIN METHOD OF TREATMENT—RADICAL SURGERY AND POST-OPERATIVE RADIOTHERAPY. TOTAL CASES, 790

Years after treatment	Number of cancer deaths	Number exposed to risk	Chance of dying in any one year	Survival rate
1	232	789.5	.294	70.6%
2	156	555.5	.281	50.8%
3	65	395	.165	42.4%
4	51	323	.158	35.7%
5	25	267	.094	32.4%

In the period 1941-45 the total number of cases, "operable" and "inoperable", referred to the Royal Infirmary was 1,345 and the five-year survival rate of 43.1% is higher than that of the period 1935-40. Statistical examination shows that the difference is significant.

TABLE XI.—SURVIVAL RATE OF ALL "OPERABLE" AND "INOPERABLE" CASES REFERRED IN THE PERIOD 1941-45. MAIN METHOD OF TREATMENT—SIMPLE MASTECTOMY AND POST-OPERATIVE RADIOTHERAPY. TOTAL CASES, 1,345

Years after treatment	Number of cancer deaths	Number exposed to risk	Chance of dying in any one year	Survival rate
1	261	1,345	.194	80.6%
2	159	850.5	.187	65.5%
3	82	509.5	.161	55.0%
4	35	256.5	.136	47.5%
5	9	97	.093	43.1%

CARCINOMA BREAST WITHOUT DISTANT METASTASES

When the cases with clinical or radiographic evidence of distant metastases are excluded from the total patients seen in the period 1941-45 the five-year survival rate is 50.1%.

TABLE XII.—SURVIVAL RATE OF ALL "OPERABLE" AND ALL LOCALIZED "INOPERABLE" CASES IN THE PERIOD 1941-45. MAIN METHOD OF TREATMENT—SIMPLE MASTECTOMY AND POST-OPERATIVE RADIOTHERAPY. TOTAL CASES, 1,146

Years after treatment	Number of cancer deaths	Number exposed to risk	Chance of dying in any one year	Survival rate
1	139	1,146	.121	87.9%
2	119	784.5	.152	74.5%
3	75	489.5	.153	63.1%
4	33	249.5	.132	54.8%
5	8	94	.085	50.1%

This finding is all the more remarkable when it is borne in mind that not all those cases were treated by simple mastectomy and radiotherapy. Even amongst the operable cases some were too elderly and others suffering from advanced cardiac disease, pulmonary tuberculosis, advanced rheumatoid arthritis, &c., were quite unsuitable for treatment. It will be recalled too that a number of deaths were actually added to the tables so as to allow for any possible post-operative deaths in cases where the operation was performed outside the Infirmary.

COMPARISON WITH OTHER CENTRES

One of the best-known and most reliable series in the literature is that of Harrington of the Mayo Clinic. His figures probably represent the best results obtainable by surgery in a large number of

cases. Unfortunately the extent of selection is not indicated and it should be noted that only treated cases are included. Some degree of selection may be presumed, for in 40% of the cases microscopic examination of the axillary glands did not show involvement.

The best results from surgery published in this country are those of Gordon-Taylor. His results are far superior to those of any other surgeon in this country and it should be noted that they are the results of an individual surgeon and not those of a hospital.

Truscott's figures are of particular interest because the results are based on a group of cases very comparable to those accepted as "operable" in this paper (*see* Stages I, II and III in his article), and also because they refer to all such cases referred to the Middlesex Hospital in the period 1926-35. It is unfortunate that the results of the treatment methods used since 1935 are not given and it is to be hoped that the publication of these will not be long delayed for such figures indicate the true value of treatment methods far more clearly than the publications of individual surgeons.

The figures of Haagensen and Stout show the five-year survival rate to be expected when radical surgery is the only method of treatment and all cases coming to a large general hospital are included.

TABLE XIII.—COMPARISON OF SURVIVAL RATES

		3-year	5-year	10-year
Harrington (Mayo Clinic)	Treated cases	60.9%	47.6%	31.1%
Gordon-Taylor (Middlesex Hospital)	Treated cases	55.0%	51.9%	43.5%
Truscott (Middlesex Hospital) (1926-35)	All "operable" cases	—	28%	14%
Edinburgh (1941-45)	All "operable" cases	71%	56%	—
Haagensen and Stout (Presbyterian Hospital)	All cases referred	—	22.2%	—
Edinburgh (1941-45)	All cases referred	55%	43%	—

Direct comparison of results is always difficult but the above figures indicate that the method of treatment now in use in Edinburgh has given results which will bear comparison with any other published figures and they give support to the view that the hypothesis underlying the method of treatment is sound.

PRESENT TREATMENT METHODS

The technique of simple mastectomy and post-operative radiotherapy is being continued with the addition of ovarian irradiation which has been added with a view to influencing distant metastases.

TECHNIQUE OF SIMPLE MASTECTOMY AND POST-OPERATIVE RADIO THERAPY

The method of treatment is a combination of two procedures which must be co-ordinated if the best result is to be obtained.

The following points are of importance in the surgical aspect of treatment:

(1) Pre-operative preparation by iodine is contra-indicated because it lowers the skin tolerance to radiotherapy.

(2) The skin incision and the undermining of the skin flaps should be as limited as possible so that tissue spaces outside the area to be irradiated will not be contaminated with malignant cells liberated during the operation.

(3) Excessive skin should not be removed for tension on the skin flaps may be associated with failure of the wound to heal and delay in the application of radiotherapy. Tightly stretched skin flaps do not tolerate radiation well. Skin grafting does not overcome the difficulty, for grafts do not tolerate X-ray treatment well.

(4) Where the primary tumour is mobile on the pectoral fascia, the fascia should not be removed as this promotes fibrosis of the pectoral muscle. If the tumour is firmly fixed to the pectoralis major, the muscle should be removed together with the breast.

(5) If there are no palpable axillary glands no dissection should be performed, but superficial mobile glands in the subpectoral region and outside the axillary fascia may be removed. Any further dissection of the axilla will defeat the whole purpose of the treatment method advocated.

(6) If the patient is very stout it is better to carry out a radical operation because in stout patients it is difficult to deliver an adequate dose of X-rays to the axilla.

(7) Supraclavicular glands should never be removed because these glands are easily and effectively dealt with by radiotherapy.

(8) Adhesive plaster should not be applied to the skin after the operation because this lowers the tolerance of the skin to radiation.

The following points are of importance in post-operative treatment by radiotherapy:

(1) Only one full course of X-ray treatment should be given. The practice of repeated courses at intervals of three to six months has no place in the treatment of any form of malignant disease where

cure is to be attempted and is just as illogical as partial removal of a tumour at intervals of three to six months.

(2) X-ray treatment should be commenced as soon as possible after the operation: the usual interval is two weeks.

(3) The chest wall must be treated by tangential or glancing fields so as to avoid lung fibrosis.

(4) An adequate dosage must be given and in Edinburgh the patients receive a minimal tumour dose of 3,750 r in a period of three weeks.

(5) The X-ray apparatus must be sufficiently powerful to deliver an adequate depth dose in the axilla and it is doubtful if effective radiotherapy can be given with an apparatus of lower voltage than 250 kV.

CONCLUSION

An account has been given of the method of treatment of breast carcinoma now in use in Edinburgh and the results so far as they can be ascertained have been presented. In a few years still more valuable figures will become available.

The results obtained support the view that by not dissecting the axilla the risk of dissemination of cells is reduced, and that radiotherapy is more effective than surgery in the treatment of the axilla. Further evidence of the effectiveness of radiotherapy in the treatment of breast cancer is obtained in the localized (see p. 126) but "inoperable" cases. In those cases there was gross disease present when the X-ray treatment was given and yet at the end of five years 24.6% of the patients were alive. This result is comparable to that obtained by radical surgery alone in all "operable" and "inoperable" cases coming to a large general hospital.

Radiotherapy has been substituted for surgery in the treatment of the axilla and, therefore, a high standard of radiotherapy is essential. Before the method is more widely adopted it is important to appreciate that simple mastectomy and a low standard of radiotherapy will be associated with results poorer than those obtained by the radical operation without any radiotherapy.

Finally it remains for me to acknowledge the co-operation of the surgical staff of the Royal Infirmary without whose support this investigation could never have been carried out.

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Sir Stanford Cade: To assess the efficacy of treatment it is important to consider the incidence and mortality of the disease. In cancer of the breast the incidence has risen consistently. Between 1935 and 1945 it has increased year by year and in the total period (ten years) 76,430 women died of this disease in England and Wales; the number of deaths in 1945 was 7,291 or over 20% of the total deaths from cancer in women (38,798).

This increase in mortality and in incidence suggests that a review of the present-day methods of treatment is desirable. Such a review should correlate the natural history of the disease with the results of various methods of treatment.

Cancer of the breast as a cause of death is registered in increasing numbers as age advances; the peak is reached in the five-year period 55 to 60 years of age and then declines slowly. I have therefore chosen 55 years as the age at which to consider expectation of life in connexion with cancer of the breast. In comparison with all other sites of cancer (except skin), the breast is the most favourable, that is, the least rapidly lethal site—and this should affect seriously the choice of the method of treatment.

Several authorities, both in this country and in the United States, have computed the expectation of life in untreated cases, of which there is, unfortunately, no lack. The mean duration is 39.3 months, that is, three years and three months. It seems that the "three-year survival", sometimes taken as a measure of success, is less than the natural expectation of life in the untreated case.

To appreciate the achievement or accomplishment of treatment Professor Major Greenwood (1926) investigated the expectation of life of a woman 55 years of age under various conditions. On actuarial estimation the normal expectation of life is 18.87 years; with untreated cancer of the breast it is reduced to 3.8 years. If treatment is given under average conditions, expectation of life is 5.78 years and with treatment under best conditions it is raised to 12.93 years.

What are the best conditions and how do these differ from the average conditions? "Best" or "average" depends on two factors which are interdependent and cannot be separated.

(1) The stage of the disease. (2) The type of treatment.

The best case can be ruined by inadequate or ill-conceived treatment; and conversely, no treatment, however excellent, will make much difference in a bad case. These two factors are, in my opinion, the key to an unbiased assessment of treatment methods.

cases. Unfortunately the extent of selection is not indicated and it should be noted that only treated cases are included. Some degree of selection may be presumed, for in 40% of the cases microscopic examination of the axillary glands did not show involvement.

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(8) Adhesive should not be applied to the skin after the operation because this lowers the tolerance of the skin to radiation.

The following points are of importance in post-operative treatment by radiotherapy:

(1) Only one full course of X-ray treatment should be given. The practice of repeated courses at intervals of three to six months has no place in the treatment of any form of malignant disease where

In such cases radiation is the weapon of choice and pre-operative radiation is, on common-sense grounds, from clinical observation of cases and on histological studies, the method of choice. Radium by moulds or plaques, or the more flexible and equally suitable method of X-rays, leads to regression of the disease and transforms a percentage of cases into Stage I cases, suitable for surgery; in other cases the progress of the disease is arrested and life prolonged by many years.

It is necessary to define more precisely what is meant by pre- and post-operative radiation. Pre-operative radiation aims at sterilization of the active neoplasm in the breast, in the skin over the breast and in the axillary glands. Careful histological studies of breasts amputated at various periods after irradiation have been made by many pathologists and show obvious effects familiar in other sites such as the uterus and skin. In contrast post-operative radiation deals, or should deal, with extensions of the disease beyond the anatomical area covered by the radical amputation, namely, the supraclavicular and anterior mediastinal or retrosternal glands and the flaps of skin lifted at the operation. Unless the case is inoperable (in which case it should not be operated), post-operative radiation deals with potential disease—a somewhat speculative treatment. Pre-operative radiation, on the other hand, treats obvious palpable neoplasms. Such treatment is of benefit, not only as a pre-operative procedure, but in a proportion of cases as a sole therapeutic measure, which has been abundantly proved and is, of course, the accepted method in the treatment of recurrences.

There is, in my opinion, an obvious difference in the usefulness of both these methods and a recent statistical analysis by Dr. Stoll of 448 cases of carcinoma of the breast, treated at Westminster Hospital between 1930 and 1942, supports this contention. He found that in Stage I cases post-operative radiation gave a five-year survival of 53%, and pre-operative radiation a five-year survival of 73%. The figures given by E. Berven from the Radiumhemmet, Stockholm, are even more striking: with fixed axillary glands, the five-year survival with post-operative radiation was over 9.7%, whereas with pre- and post-operative treatment it rose to 32%.

Local mastectomy.—The value of local mastectomy is clear cut—it removes the breast and primary tumour. It does not touch the axillary contents and if disease is present there, palpable or non-palpable, operable or inoperable, actual or potential—there the disease remains. As a clinician I am not attracted by the idea of removing part only of a cancer, be it in the breast or elsewhere, if I can, with impunity to the patient, remove all of it, and as the operative mortality of a radical mastectomy is small, and the morbidity limited, I prefer to offer the patient, if otherwise suitable, the bigger and, in my view, the better of the two operations. Simple mastectomy is suitable in the aged, for the removal of a fungating mass, in bad surgical risks with localized disease, in cases where radiation is not available or suitable. Simple mastectomy has its value; it has, like the radical operation, definite limitations. As a routine surgical procedure, regardless of stage of disease or age of patient, it is a retrograde step and is quite unwarrantable.

In conclusion: The choice of the method of treatment should be guided by many factors. The best results following the best form of treatment are not unnaturally achieved in the best cases and so far radical mastectomy achieves this more frequently than all other therapeutic measures.

Radiation is of value:

- (1) As the sole method of treatment in Stage III cases and here the end-results following radiation are better than those following surgery.
- (2) As a pre-operative measure in Stage II cases, where improved results can confidently be expected.
- (3) As a post-operative measure, chiefly in Stage II cases.

With the better education of doctors and patients, more women will report to hospitals at an early stage—it would be a pity if this painfully achieved progress were stultified by a deterioration in our methods of dealing with the disease. If women are to be mutilated by amputation of the breast, let them at least derive the maximum benefit from such mutilation.

Mr. R. S. Handley said that he had removed the second intercostal space gland of the internal mammary lymphatic chain in 20 cases of carcinoma of the breast, and his collaborator, Dr. A. C. Thackray, had examined the material microscopically. The study had so far been chiefly a pathological one with the object of finding out how often the internal mammary glands were invaded in carcinoma of the breast; and the second intercostal space had been chosen because it contained the largest and most constant gland of the chain. In the 20 cases examined, no glandular involvement had been found in 6 patients; both intercostal and axillary glands were invaded in 9; in 3 cases only the axilla was involved and in 2 cases only the intercostal gland. It was easy to open the intercostal space but more difficult to find the gland, though matting of the tissues round the internal mammary artery usually betrayed invasion of the space. The largest invaded gland he had encountered had been the size of an orange pip, the smallest the size of a pin-head. Though clinical recurrence in the second intercostal space was not very common in these days, it was difficult to believe that carcinoma cells lying almost on the pleura were harmless. If the intercostal glands were invaded, the patient could not be cured by surgery alone and additional radiotherapy was necessary. He thought that if the axilla was clinically free from invasion or showed only small mobile glands, the operation should start with a second intercostal space biopsy. If a rapid frozen section showed the space to be free from growth, a radical mastectomy should be done. If, however, the space was invaded, the operation should be limited to a simple mastectomy with additional removal only of such of the axillary contents

Of all factors affecting prognosis, *stage* of the disease is the most important. A distinction should be made between stage and duration, as sometimes a long history is of favourable prognostic significance, as it implies a slow progress and a lower degree of malignancy. Neither site nor size of the tumour, nor age of the patient is of such importance; the physiological state of the breast, pregnancy, lactation or menopause and the histological variety, are significant, but none of these factors—size, site, length of history, histological variety or clinical type—is of such crucial importance as the *stage* of the disease. It is therefore essential to have a clinical classification. Of these, there are many—all suffer from the defect of attempting too much. Some classifications are of theoretical value only. I suggest the following:

Stage I = Tumour of the breast only.

Stage II = Tumour of the breast + skin changes and/or axillary glands.

Stage III = Tumour of the breast + supraclavicular glands or contralateral axillary glands or fixation to pectoral fascia.

Stage IV = Skeletal or visceral metastasis.

Stages I and II are anatomically within the area covered by radical mastectomy; Stage III is beyond surgical excision and Stage IV suitable only for palliative measures by radiation or endocrine therapy.

The zone of demarcation, between good and evil prognosis, between fair or poor chance of survival, is the clinical state of the axillary glands. It is, of course, agreed that sometimes clinically non-palpable glands show histological invasion, and, conversely, palpable enlarged glands show, occasionally, inflammatory changes only—but on the whole the presence or absence of palpable and clinically malignant axillary glands is the best guide to the future of the patient.

It is my contention that in Stage I of the disease the best method of treatment is radical mastectomy. This contention is supported by much evidence and it may suffice amongst the wealth of material to choose a few published results. Thus Truscott (1947), in an analysis of 836 cases at the Middlesex Hospital, found at the end of five years 64% survival in Stage I and only 31% survival in Stage II. A. B. McGraw (1947), in 412 patients, states that of those with axillary nodes involved only 29.6% survived five years, whereas of the patients without involvement of axillary glands 64% survived five years. Table I shows these figures and those of Sir Gordon Gordon-Taylor (1938), Geoffrey Keynes (1939), University College Hospital (1937), the Ministry of Health and my own series up to 1935, reported in 1940.

TABLE I.—EFFECT OF STAGE OF DISEASE ON 5-YEAR SURVIVAL

	Stage I	Stage II		Stage I	Stage II
	%	%		%	%
Truscott	64	31	University College		
McGraw	64	29.6	Hospital	69	30
Gordon-Taylor ..	86	40	Ministry of Health	65	30
Geoffrey Keynes	71	29	Stanford Cade ..	87	29

All these reports show very high five-year survival rates in Stage I cases (Table I).

Post-operative radiation in this group of cases as an additional measure is, in my opinion, of doubtful value. In other words, results do not appear to be improved by adding radiation to the skilfully performed radical mastectomy in this stage, viz. Stage I, that is in the best type of case. This does not mean that I am prepared to deny the patient radiation; and, as a matter of fact, providing radiation is carefully given, there is no reason to deny it to the patient. The mortality of the radical mastectomy is negligible. It was considered important to find out the mortality of radical mastectomy: for this purpose all the teaching hospitals in London and in nine provincial universities were circularized and I am indebted to twenty-two colleagues for the trouble taken to provide the mortality figures. Any death within one month from the operation was considered as an operative mortality. Of 11,014 radical mastectomies 182 patients died, 1.65%. The mortality was higher, 1.9% in the hospital series, where the operations by experienced surgeons and by those under training were pooled together; it was a little lower 1.1% when the mortality in the hands of "master surgeons" only was analysed (3,866 radical mastectomies with 44 deaths). It is emphasized that the risk to life from radical mastectomy is *very low*.

It is now important to draw attention to the limitation of usefulness of this operation. It gives the best results in Stage I. The results in Stage II are much worse and by itself the operation offers a chance of five-year survival in about 20% to 30% of cases only. Stage 2 should be analysed. It comprises the patients with enlarged axillary glands and those with skin invasion. There are three types of skin invasion: (1) The direct spread and fungation—it is the least malignant; (2) the diffuse invasion with oedema—the pigskin or peau d'orange type—it is of grave significance; (3) the invasion of the skin by discrete nodules so admirably described by Sampson Handley—it is a death sentence.

I wish to emphasize the incalculable harm done by radical mastectomy in many cases, with the last two types of skin involvement. The operation in these patients does not prolong life; it seems, in some cases, to open wide every channel for the uncontrolled spread of the disease. Unfortunately, all radiotherapy departments are familiar with cases where within a few weeks or months following operation, the chest wall is covered with numerous metastatic nodules, which break down and cause more suffering than the original disease.

Section of Anæsthetics

President—JOHN CHALLIS

[December 5, 1947]

Posture in Anæsthesia. [Summary]

By J. K. HASLER, M.B.

POSTURE in anæsthesia is a subject about which little has been written except for a few papers which have recently been published in America. During the past few years I have heard of several unfortunate sequelæ as the result of faulty posture on the operating table. Most of these cases were nerve palsies and as little seems to get into print about them I wonder whether they are commoner than is supposed.

In the anæsthetic room.—With adult patients our chief concern should be to see that they are comfortable. Many, however, arrive from the ward with one thin pillow which is often placed under the shoulders, thereby extending the head. When asked if they would like their heads raised they give a deep sigh and say "Yes". Elderly or obese patients dislike lying flat and appreciate an extra pillow. Nor is there any reason why they should be denied one. With younger patients there are two points to observe. First, those who have had adequate premedication arrive in the anæsthetic room asleep. They are often curled up on one side with the head partially muffled in blankets. This is an excellent position in which to induce anæsthesia with nitrous-oxide by means of a facepiece held just above and near to the patient's face. They should not be waked up by being rolled on to the back. The second point concerns small children who come to the anæsthetic room conscious. Many arrive sitting upright on the trolley and it is in this position that anæsthesia should be induced if they show any objection to lying down.

In the theatre.—We now pass to the operating theatre. In 1932 Dutton suggested that for operations on the abdomen a pillow should be placed behind the patient's knees to flex the thighs and relax the abdominal muscles. Then in 1943 Altschule investigated various factors in surgery which interfered with respiration. Among these was the Trendelenburg position which, at an angle of 22.5 degrees, was found to impair respiration by 17%. He says: "The decreases in volume of functional residual and reserve air in the Trendelenburg position are significant in two respects: (a) They indicate that this posture favours atelectasis by collapsing about 20% of the lung, and (b) they indicate that the intrapleural pressure is less negative than normal in the head-down position." In other words this position impairs return of blood to the heart. Prolonged use of this position is therefore unwise in patients with respiratory and circulatory depression including those with shock. Finally in 1946 Case and Stiles investigated the effect that various postures had on vital capacity of respiration. The subjects examined were all conscious and could therefore co-operate to the full. They found that the most unfavourable positions for patients on the operating table are the Trendelenburg, the lithotomy, and those in which bridges or rests are used. Patients operated on in these positions should remain in them for the minimal time commensurate with good surgery. They also suggested that as their subjects were conscious the figures are probably better than for patients under anæsthesia.

Dorsal position.—In this position the patient lies on his back horizontally with his head more or less in line with the trunk. Some form of restraint for the arms is necessary to prevent them slipping down at the sides of the table. A common habit is to place the hands palms downwards under the buttocks. This is unfortunately not without risk. Elderly patients, after a long operation, have sometimes developed gangrene of the fingers from pressure of the buttocks. What other means have we to fix the arms? One is Patterson's arm clamp consisting of two wide strips of metal whose curved ends hold the arms to the patient's side. Another device is a broad strip of canvas placed transversely across the table beneath the patient with straps and buckles at the outer ends to fasten round the wrists. An even simpler device is an ordinary roller towel also laid transversely beneath the patient. The ends of this are brought up over the patient's arms and tucked under the trunk thus providing restraint for the arms without undue pressure. Sometimes the arms are kept raised above the head. This position should be avoided as damage may be caused to the two lower branches of the brachial plexus by stretching against the first rib (Klumpke's paralysis). In the past year I have heard of two brachial palsies resulting from this posture. In one the anæsthetist withdrew an arm for intravenous therapy and kept it above the head for the rest of the operation. The result was a typical Klumpke's paralysis. The other case is less easy to explain as the upper branches of the plexus were affected producing an Erb's paralysis. Apparently the arm was not raised higher than the shoulder but was allowed to sag backwards. The table was also tilted sideways with the possibility that the head became

as were within easy reach. Radiotherapy must deal with the deposits within the chest and might as well cope with the apex of the axilla.

Dr. F. M. Allchin emphasized the value, as a pre-operative measure, of irradiation of tumours of the breast in Stage II cases. Those who have been fortunate enough to see the results of such treatment could not but fail to be impressed. The gross changes produced by interstitial radium treatment so ably carried out by Keynes and a few others had been repeated with X-rays. Many breasts thus irradiated had shown by histological examination after removal a complete absence of active cancer cells. These were what might be termed the more radiosensitive tumours. In the more resistant types shrinkage of tumours is not so marked and many attenuated malignant cells are found throughout the breast after irradiation. In both types the fact must be recognized that there are still potentially malignant cells remaining which may start into a period of activity at some future date. Hence the necessity for the operative procedure after irradiation before such activity begins. These remarks applied with even greater emphasis to the axillary glands which in his (Dr. Allchin's) technique are irradiated at the same time as the breast. As it was more difficult to remove all traces of malignant cells from metastatic glands the necessity for the clearance of the axilla became even more apparent.

Dr. Allchin added a plea for the education of practitioners and even of surgeons in the importance of establishing a diagnosis on every lump in the breast. The number of confident diagnoses of fibroadenoma and cyst in the breast which subsequently turned out to be carcinomata was far too great. Diagnosis on clinical grounds alone was too unreliable and should always be confirmed by histological findings.

[January 7, 1948]

Pathological specimens were shown as follows:

Intussusception of Ascending Colon from Carcinoma.—Mr. HAROLD DODD.

(1) Fibroma of Lung Removed by Lobectomy. (2) Ulceration of Œsophagus Due to Indwelling Ryle's Tube. (3) Photographs of Stomach Four Months after Ramstedt Operation.—Mr. IVOR LEWIS and Dr. J. H. HEGGIE.

Adenomyoma of the Duodenum (Hamartoma).—Mr. A. S. TILL.

(1) Post-operative Thrombosis of Deep Veins. (2) Neurinoma of the Vagus.—Mr. R. S. MURLEY.

(1) Pedunculated Intraperitoneal Metastases from Leiomyosarcoma of Stomach. (2) Obstruction of Ileum from Metastasis from Carcinoma of Colon. (3) Two Abnormalities of the Ileocæcal Valve. (4) Multiple Ulcerations of the Alimentary Tract. (5) Multiple Myelomatosis.—Mr. N. M. MATHESON and Dr. A. G. SIGNY.

Acute Non-specific Ileitis.—Mr. STANLEY AYLETT.

Lymphosarcoma of Ileum with Intussusception.—Mr. C. NICHOLAS.

Resection of Pancreas for Carcinoma.—Mr. L. P. ALLAN (for Mr. HAROLD DODD).

Extrarenal Hypernephroma.—Mr. FRANK FORTY.

Aortic Abdominal Aneurysms (2 Cases).—Mr. W. W. DAVEY.

Wilms' Tumour Treated by Radiotherapy.—Mr. J. P. HAILE (for Mr. ELLISON NASH).

Neurofibroma of Stomach.—Mr. F. N. GLOVER.

Intussusception from Secondary Bronchial Carcinoma.—Mr. LACEY (for Mr. D. H. PATEY).

magnus muscle by pressure on the long thoracic nerve, a condition sometimes seen in porters who carry heavy loads on the shoulder. They may also interfere with the venous return of the arm especially if it is supported at right angles for intravenous therapy. Recently I noticed an arm in this position assuming the mottled appearance of venous congestion and when I had eased the shoulder piece the arm rapidly regained its normal colour. A drip transfusion may become slow and stop under similar conditions. The explanation seems to be that pressure on the clavicle by the shoulder piece causes compression of the subclavian vein where it passes between the inner end of the clavicle and the first rib. The third method of fixing the patient in this position is by means of iliac crest supports. These are like modified shoulder pieces at the side of the table which press into the loins above the iliac crests. They should be fixed into position by the anæsthetist or surgeon as the nurses find the task difficult. Two disadvantages are associated with them. First, they are designed for use with the "Bart's" pattern of operating table and cannot be used on other tables unless modified. Second, they tend to bunch up the abdominal fat over the mid-line which may make operation difficult in stout subjects. Before leaving this position there are two points to consider. During spinal anæsthesia it is important to have a slight tilt head downwards to safeguard cerebral circulation. It is also important that the anæsthetist should be able to get the patient into this position in a matter of seconds in cases of sudden vomiting. The cases I have in mind are those with intestinal obstruction and those who come to the theatre with a full stomach.

Lithotomy position.—Case and Stiles found that the loss to vital capacity in this position was 18% and I was surprised to find this figure greater than that for the Trendelenburg position. Fortunately most patients needing this position do not require deep anæsthesia and can be operated on under low spinal or pentothal. Whatever pattern of support is used should hold the legs up as high as possible. This produces less pressure on the abdomen by the flexed thighs and it reduces the cramp of which patients sometimes complain when they are conscious. Sometimes a patient under general anæsthesia develops an ankle clonus when moved from the dorsal position into the lithotomy position. This is due to the patient's posture for the straps supporting the legs cause a sudden dorsiflexion of the feet when the patient is shifted, especially if this is done with a jerk. When the foot is extended the clonus stops and will not recur if the foot returns to its former position gently. Years ago this was called an ether clonus but I have seen it occur under pentothal and nitrous-oxide.

Lateral and kidney position.—With this position my chief worry is how best to place the patient's lower arm. If it is pulled too far backward he tends to roll on to his face and if pulled too far forward he tends to roll on his back. In the mid-way position the weight of the body presses on the under arm and often obstructs the venous return and in a short time the arm becomes mottled. If the patient is conscious he keeps shifting his shoulder to ease the discomfort and the surgeon is apt to complain. I have never seen any arm lesion result from this position but have an uneasy feeling that it may. I sometimes give pentothal to patients in this position and have wondered whether there would be delay in the drug reaching the general circulation but so far this has not occurred. Regarding the loss in vital capacity Case and Stiles found this was 10% for the left lateral and 12% for the right lateral position. With the bridge of the table raised for nephrectomy the loss is increased to about 14%.

Upright posture.—Most of the anæsthetics we give to patients in this position are for dental operations. The agents, at any rate for adults, are nitrous-oxide or pentothal though opinion is divided about the advisability of using the latter drug. The position of the patient is important. The head and trunk should be in alignment with the body nearly upright. Knees should be bent to a right angle with feet resting on the floor of the chair. In this position there is less chance of the patient slipping down while unconscious. If the feet are extended and resting against the bar at the end of the chair it gives him something to push against while under gas. The upright position must also be considered in relation to lung abscess. Two recent American textbooks make reference to the occurrence of lung abscess after operations on the nose and throat especially tonsillectomy. Here the complication is rare, the chief difference between us and the Americans is that many of their tonsillectomies are performed with the patients in the sitting position. In this posture septic material may drop downwards and enter the lungs through a larynx rendered insensitive either by local or general anæsthesia. Another point, chiefly of historical interest, concerning this position is on the use of chloroform. In the days when this drug was administered more frequently than it is now anæsthetists were warned of the danger of giving it to patients in the upright position. Both Hewitt and Hadfield in their textbooks issue this warning. Under chloroform the blood-pressure falls and there is the danger of sudden collapse or even death in this position.

Spinal anæsthesia.—The first point to emphasize is that the posture of the patient in the period immediately after the drug has been injected is the most important factor in determining distribution of the drug. It is simply a matter of gravity. If a heavy solution is introduced into a vessel containing a lighter solution the heavy solution will sink to the lowest

extended laterally away from the affected side and kept the tissues of the neck under tension. At any rate the patient had an upper arm palsy which lasted for eight weeks. If intravenous therapy is required during operation an arm should be extended at right angles and supported by a board. If this interferes with the surgeon the arms should be flexed with elbows resting on the sides of the table and hands flat on the sternum. The pyjama jacket can be turned back over the arms and its loose ends tucked under the elbows. Thus the arms are under control and it is not unduly difficult to get one out and replace it for intravenous therapy.

Pulmonary embolism is a perpetual bugbear to the surgeon and blame has recently been thrown on the veins of the calf as offenders in this respect. In the dorsal position the calves press directly on to the table and the veins of that area may become obliterated for a long period. Professor Lambert Rogers (1946) has prevented this by placing support behind the ankles and thus taking pressure off the calves. He has adopted this technique for over nine years and up to 1946 he had had no case of embolus in patients so treated. Except with tall patients the feet should not project beyond the end of the table. A case once occurred in which the table was moved close to the theatre window during an operation. Nobody saw that, at the end of the move, the patient's feet which projected beyond the table were touching a hot radiator with the result that severe burns were produced on the feet. In tall patients where projection of the feet is unavoidable one should place some soft material behind the heels to prevent pressure from the table.

Modification of the dorsal position is used in cholecystectomy. By raising a bridge in the centre of the table the trunk is extended and the ease of operation is increased. This is of more advantage to the surgeon than to the patient. In the paper to which I have referred, Case and Stiles found that the vital capacity is reduced by 12.5% in this position. In practice this position is tolerated by patients without undue difficulty but sometimes there are anxious moments. I once had to anesthetize a fit man of about 70 for removal of the gall-bladder. Induction was uneventful and when he was on the table the bridge was raised and the surgeon started work. During operation he became increasingly cyanosed despite added oxygen and his pulse became rapid and feeble. At length I told the surgeon we had better get him back to bed as soon as possible. By that time the gall-bladder was out and the surgeon was ready to close the peritoneum so the bridge was lowered. Within five minutes the pulse had settled down, the patient's colour had returned to normal, and operation was concluded without worry. I am quite convinced that the extended posture was responsible for this patient's distress. Another modification of this position often occurs after operation for hernia. The patient is lifted up and dropped upon an upturned porringer for the easy application of a spica bandage. Extension of the lower spine while the muscles are relaxed may give rise to trauma and I have seen a patient complain bitterly of backache after repair of hernia. As I can think of no reason to connect either the general anaesthetic or the operation with the backache I can only suppose that it was caused by the change of posture.

Trendelenburg position.—This is another modification of the dorsal position in which the table is tilted and the patient's head placed lower than the trunk. Originally the name was given to a tilt of 45 degrees but it now covers all degrees from a slight tilt to the extreme degrees used in operations on the pelvis. Case and Stiles found that diminution in vital capacity with this position was 14.5%. This was for a tilt of 20 degrees. In Altschule's paper the tilt was 22.5 degrees and impairment of respiration found to be 17%. While considering the effect of this position on respiration we may remind ourselves that the rocking method of artificial respiration relies on a tilt head downwards to empty the lungs. It would be interesting to have figures for the loss in vital capacity for a patient deeply anesthetized, at a tilt of something over 45 degrees, and with large packs in the upper abdomen. Personally I dislike a steep tilt especially in fat patients as I find it produces heaving respiration. I encourage the surgeons with whom I work to use as little tilt and for as short a time as possible. Other problems raised by this position are with the means employed to keep the patient fixed on the table. Two methods are in common use and a third which is less well known. In the first of these the patient's legs are fixed by straps round the ankles and the end of the table is dropped to a right angle thereby flexing the knees. If the table is tilted before the legs have been bent the patient may slide slightly and the bend at the knees may not correspond with the bend in the table. I know of two cases in which this position caused trauma. In one case pressure from the edge of the table produced paralysis of the external popliteal nerve with a resulting foot drop which lasted for two months. In the other case damage occurred to the popliteal artery and the result was gangrene and amputation. This was presumably due to the kinking of an already diseased artery for a long period. The other common method of supporting the patient is by means of shoulder pieces. These vary in pattern with different tables. Personally I feel that the anaesthetist should fix them or at any rate make the final adjustment. If left to the nurses they are often placed at different levels and at varying points of contact with the shoulders. Faulty application of the shoulder pieces may lead to nerve palsy. If placed too close to the neck pressure on the upper part of the brachial plexus may produce Erb's paralysis. They may also paralyse the serratus

Dr. H. W. Loftus Dale said that he, in common with Dr. Hasler, had observed the thin, small pillow on the theatre trolley, but liked it. It gave him the opportunity of saying to the patient "you are not comfortable, Nurse, get this patient another pillow", thus getting on good terms with the patient at once.

In cases where complete muscular relaxation was produced by curare or spinals, the use of a pillow to support the lumbar curve lessened ligamentous strain, so diminishing the tendency to post-operative backache.

Abdominoperineal excision of the rectum by the synchronous combined method done on an ordinary operating table necessitating the employment of a steep Trendelenburg tilt and the lithotomy position, plus a few abdominal packs, made it almost impossible for the anæsthetist to maintain adequate tidal exchange however hard he might try to assist respiration.

The prone position with pillows under the pelvis and legs abducted enabled hæmorrhoidectomy to be done under a "saddle area spinal" with much less congestion and hæmorrhage than is associated with the more commonly used lithotomy position.

Dr. R. J. Minnitt said that the subject of the posture of the patient was deemed so important that a whole chapter had been devoted to it in Ross and Fairlie's "Handbook of Anæsthetics" since it was first published, and this had been further elaborated by Dr. Gillies in later editions of the "Textbook".

There were three points he wished to mention. First, with regard to the bridge for the gall-bladder operation. One of the surgeons with whom he worked, experimenting upon himself, lay on the operating table for some time with the bridge up. The intense backache he endured afterwards led him to decide never again to operate upon a gall-bladder, using a bridge. Dr. Minnitt had been agreeably surprised as to how well this could be done, given good anæsthesia.

Secondly, he was once giving an anæsthetic to a patient in the lithotomy position, the arms being folded upon the chest. The surgeon gave the patient a push to correct the position, and in doing this one of the arms dropped over the edge of the table. Had the occurrence not been seen by a probationer a disastrous result might have ensued.

Thirdly, he had seen a patient fixed up in a Clover's crutch, about to undergo a gynaecological operation in a private house, lifted on to the end of a portable table, which tipped up and deposited her on the floor.

Dr. G. S. W. Organe instanced a large hospital with which he was associated where, as a result of persistent pressure from the anæsthetists, only one surgeon still insisted on the use of the gall-bladder rest, and where the gynaecologists themselves limited the degree of tilt in the Trendelenburg position. He mentioned, also, having seen Italian gynaecologists return the patient to the horizontal position before suturing the peritoneum, and abdominal surgeons apply pressure to the abdomen before drawing tight the last peritoneal stitch, in both cases with the idea of limiting the amount of air left in the peritoneal cavity.

Dr. H. J. V. Morton said that Dr. Hasler had rightly stressed the respiratory embarrassment which might be caused by the Trendelenburg position. The experimental work he quoted was of great interest in this respect. The whole question should, however, be reconsidered with due regard to modern anæsthetic practice. It could be shown that "assisted respiration" with a closed circuit apparatus effectively compensated any respiratory inadequacy brought about by the Trendelenburg position.

Mention should also be made of the use of posture in controlling sputum in thoracic surgery. For years it had been the custom to use the lateral head-down position in cases where bronchial occlusion was impracticable. Did the newer prone head-down position really offer noteworthy advantages? The muscles of respiration seem to fatigue readily in some cases in this position. Was there enough clinical evidence for the assertion that complications due to the passage of sputum to the good side were significantly less frequent with this method?

Dr. H. K. Ashworth said that he felt somewhat disquieted by Dr. Hasler's account of the opinion given to him by an official of one of the Medical Protection Societies on the legal responsibility of an anæsthetist for accidents arising from posture during anæsthesia. In his (Dr. Ashworth's) opinion no anæsthetist should ever neglect his primary duty of providing safe anæsthesia in order to place the patient in the posture required for operation. It should be a matter of courtesy, and not of responsibility, for the anæsthetist to perform this function. When the patient was arranged in the required posture for any particular operation, the surgeon was always asked if he was satisfied with the arrangements before the operation started, and Dr. Ashworth then felt that the surgeon's acquiescence discharged the anæsthetist's legal responsibility in this matter.

In one hospital in which a Resident Anæsthetist took part in the preparation of the patient, death took place while he was so engaged, and a rule was passed that in no circumstances would the anæsthetist take part in the preparation and posture of a patient for operation.

One unusual posture in which he was called upon to anæsthetize patients was sitting almost upright for the operation of cholecystectomy.

The President said that Dr. Hasler's paper displayed much common sense and information essential to the care of all patients during anæsthesia. He also pointed out that the present-day anæsthetists were called upon to do so many additional duties, such as positioning of patient, blood transfusion, supervision of tourniquets, &c., that he felt it necessary to guard against the possibility of anæsthesia becoming a minor incidence in the course of supervising the general efficiency of the theatre.

part of the vessel. If the fluids are miscible some degree of mixing will take place though it is possible to exercise some control over this. Supposing that 1 c.c. of heavy nupercaine is injected into a patient: If the patient is sitting at the time of injection and allowed to remain sitting for a few minutes low spinal anaesthesia will be produced high enough to do a closed operation on the bladder. If he lies on his side and the injection is made slowly to avoid mixing then if he remains on his side until the solution is fixed it is possible to produce unilateral anaesthesia with the underside affected. If on the other hand the injection is made with the patient on his side and immediately after he is placed on his back and given a slight tilt head downward then a bilateral anaesthesia will be produced to varying distances up the abdomen. Unilateral anaesthesia is easier to produce with a quick-acting solution like stovaine than with a slower one like nupercaine. The next point is that in my experience it is easier to perform lumbar puncture with the patient in the sitting position than on his side. I have never been able to satisfy myself why this is so. I have seen it suggested that a sandbag should be placed under the patient's loin to keep the spine straight but this would only provide a partial answer. I recently gave a spinal to a patient who was so fat that it was impossible to feel the tips of the lumbar spines while she was on her side. After several unsuccessful attempts I decided to have one try with her in the sitting position. In this posture I found it possible to palpate the spine and puncture was performed without difficulty. Another point to note is that extreme flexion of the spine is not always necessary for lumbar puncture. Sometimes I have introduced the needle too high in the space and on pushing it in horizontally have touched the spine of the vertebra below. Tilting up the needle is impossible as the tip of the spine above prevents this. By making the patient sit up slightly to extend the spine the skin over the back is relaxed and it is possible to approach the space at a slightly lower point without taking out the needle and making a second puncture. This enables the necessary tilt to be given to the needle. I have had numerous opportunities to give spinal anaesthetics to patients with fractures of the neck of the femur for insertion of a Smith-Petersen pin. It is impossible to get much flexion on the spines of these patients and only very occasionally have I had difficulty in performing lumbar puncture. The next point is that patients under spinal anaesthesia are liable to get a fall in blood-pressure and sometimes a rise in pulse-rate if their posture is changed, e.g. dorsal to left lateral position. Any change in position that is necessary should be done gently and if the patient is in a steep Trendelenburg position and the time comes to reduce the tilt it should be done in one or two easy stages rather than all at once. The reverse Trendelenburg should be avoided in these patients without first giving an intravenous injection of some pressor drug such as ephedrine or methedrine.

Miscellaneous points.—In the passage of an endotracheal tube correct position of the head is essential especially for blind intubation. Magill has taught us this for years. With regard to the prone position easy maintenance of anaesthesia is difficult unless one first passes an endotracheal tube. In the post-anæsthetic period posture is important. Elderly patients and those liable to pulmonary complications are raised in bed and not kept flat for longer than necessary. Patients in whom blood may accumulate in the throat such as tonsillectomy or dental cases should be placed on their side and kept there until round from the anaesthetic. After spinal anaesthesia patients should be kept with the feet slightly raised to prevent headache and finally those with accumulation of fluid in the air passages may have postural drainage.

Legal responsibility.—How does the anaesthetist stand in any legal action which might result because of nerve palsy or other sequela due to faulty posture? The secretary of the Medical Defence Union has kindly put the following facts before me. Each case must be decided on its own merits and there has been a tendency of recent years to blame the hospital and theatre staff rather than the surgeon. Nevertheless the responsibility for instructing the nursing staff rests in the first place with the medical staff who should keep an eye on them to see that they understand their duties. While the surgeon is usually busy getting washed and gowned or proceeding with the operation the anaesthetist is in a better position to see how the patient is placed on the table and to supervise such matters as the adjusting of shoulder pieces. In the event of an action for damages the surgeon, the anaesthetist, and the hospital may all have to appear together as defendants. In the event of a verdict in favour of the patient the anaesthetist and the hospital may well be held jointly responsible.

In conclusion I wish to express my thanks to Professor Kirk of the Middlesex Hospital Medical School for help with anatomical problems, to Dr. Forbes, secretary of the Medical Defence Union for help with the legal problems, and to those colleagues who have told me about their cases and thus helped to provide material for this paper.

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and he may have no means of defending himself against these irregularities. This is the state of a patient in deep anæsthesia.

With such a completely malleable subject how shall we determine whether or not we are carrying his gaseous exchange too far from normal? How shall we know whether by this means or by other means we may be causing him damage?

We shall, of course, carefully observe his pulse, blood-pressure and colour for any evidence of anoxia. Assuming that this evidence is absent and that the patient is of good colour can we assume that we shall be removing the carbon dioxide from his body adequately? The answer is certainly in the negative. Roth, Whitehead, and Draper [1] describe how they gave to dogs doses of pentothal three times the amount required to produce respiratory arrest. These dogs had previously been breathing pure oxygen for about an hour so that most of the nitrogen had been eliminated from their bodies. After the pentothal there were no respiratory movements in the ordinary sense although there must have been small air movements due to cardiac beats. Placed in chambers ventilated entirely with oxygen these animals nevertheless survived by what the authors describe as "diffusion respiration" for periods of about one hour. Their colour remained good provided that they were surrounded by oxygen only.

The alveolar carbon dioxide tension rose, however, to very high levels of the order of 250 mm. of mercury. Nevertheless, they did not display the serious clinical signs which might have been expected.

A patient anæsthetized with cyclopropane may be in similar case. If the anæsthesia has proceeded for an hour or two and the bag has been emptied occasionally, most of his bodily dissolved nitrogen will have disappeared. Extremely feeble ventilation will probably keep him from cyanosis. Nevertheless very great accumulation of carbon dioxide might be occurring.

The effects of high carbon dioxide pressures upon man are serious, and many papers have been written upon this subject. As in all matters of anæsthesia, however, we have to determine whether the order of the effect which we experience is sufficient to produce grave results in the condition with which we are concerned. As so frequently occurs in anæsthetic matters, it is a question of degree.

The paper of particular interest is that of Dripps [2] in which he shows that the tidal respiration during close circuit anæsthesia may fall to a very low level without necessarily exciting the anæsthetist's attention. He records cases in which spontaneous respiration was present but was so inefficient that the alveolar carbon-dioxide pressure rose to 120 mm. or more. This rise was accompanied by about a 50% rise in the systolic blood-pressure and after the cessation of anæsthesia there was a precipitate fall of this elevated blood-pressure with symptoms of collapse sometimes called "Post-cyclopropane collapse".

On the other hand Seevers and Waters [3] have remarked that during controlled respiration by hand, excessive pulmonary ventilation is often produced, particularly by less experienced anæsthetists. This excessive pulmonary ventilation will, of course, bring about a fall in the alveolar carbon-dioxide pressure. You will recall that Yandell Henderson [4] contended that surgical shock was in large measure due to a low carbon-dioxide pressure caused by hyperventilation from pain, anxiety, &c. This theory is not now generally accepted but it is usually considered that a severe fall in blood-pressure will follow periods of forced hyperventilation. Once again we must regard the matter as one of degree.

Seevers and his co-workers found effects serious, but not perhaps so grave as we might expect. In typical cases which they examined the plasma pH rose by 0.31 above the anæsthetic level when the patient was breathing spontaneously. The systolic blood-pressure fell by as much as 20 mm. of mercury and the diastolic pressure rose by about 7 mm. of mercury. Tetany was not seen but there was some rigidity and exaggeration of superficial reflexes. Seevers claimed that when normal ventilation was restored these changes were immediately reversed. In this sense their results did not suggest a development of shock as such a condition would not be immediately reversible.

We must now consider the effects of pressure within the pulmonary tree as distinct from the effects produced by pressure upon the gaseous content of the lungs.

During controlled respiration the intratracheal pressure must always be positive. There will never be a phase of negative pressure within the lungs. Forceful artificial ventilation may increase the positive intratracheal pressure very considerably and there are three ways in which this might harm our patient: (a) By impairing the pulmonary circulation; (b) by a direct action upon the venous chambers of the heart which might prevent it from filling. Either of these effects might be reflected in some deterioration of the systemic circulation.

A good deal has been written on this subject much of it based upon hypothesis only, but recently there has been renewed interest in the matter. The main reason for this renewal of interest is the introduction of breathing of oxygen under increased pressure by aviators flying at very high altitudes.

[January 2, 1948]

Artificial Respiration

By E. A. PASK, M.D., M.A., D.A.

(Department of Anaesthetics, University of Durham)

ARTIFICIAL respiration concerns anaesthetists in two ways. First we use artificial or controlled respiration upon our patient during anaesthesia. Second we are sometimes called as consultants in the matter of resuscitation for emergencies where respiration has ceased. Let us begin by discussing the possible effect of controlled respiration upon patients during anaesthesia.

How do we institute controlled respiration? If we apply to the face of a conscious man a mask connected to a bag, with suitable means for carbon-dioxide absorption, he will breathe comfortably in and out of the bag provided that we make up the oxygen consumed. If now, at a moment when he is breathing out, we attempt to inflate his lungs by squeezing the bag we shall find our effort opposed by a marked muscular effort on the part of the patient. He will resist any disturbance of the rhythm of his breathing. The mechanism involved is usually called the Hering-Breuer reflex. It is through this reflex that the state of deflation of the lungs forms at least part of the normal stimulus to inspiration and the state of inflation of the lungs forms part of the normal stimulus to expiration. The reflex requires intact function of the vagus nerve for its occurrence.

Let us now consider what will happen if we carry out the same manœuvre on a man who is in a state of apnoea following a period of voluntary hyperventilation. Before we do so, however, it may be worth while to consider briefly the nature of this state, because it is not a very simple one.

If a normal subject voluntarily hyperventilates when breathing air, after a time further respiration becomes impossible and there ensues a pause before respiration starts once more. Before the end of this pause the subject will usually have become cyanosed. His blood is deficient in oxygen but he does not start to breathe until the level of carbon dioxide has climbed once more to normal or slightly above it.

Let us now suppose that we cause a normal subject to hyperventilate voluntarily when breathing oxygen. After a time respiration ceases and at the beginning of the ensuing pause his lungs will be substantially filled with oxygen. Quickly, however, a substantial proportion of the nitrogen dissolved in his body will be released by the blood into the lungs. In this way the oxygen in his lungs becomes diluted with nitrogen as well as carbon dioxide and water vapour, but even so the pause in respiration will last longer than in the previous case and when respiration starts again the subject will usually still be of quite normal colour. The stimulus to commencement of respiration appears to be almost entirely that of carbon dioxide.

In the third case let us assume that before the hyperventilation the subject has been breathing pure oxygen for a period of about one hour. In this way some 70% of the litre or so of nitrogen dissolved in his body will have been eliminated. Now, if he voluntarily hyperventilates on pure oxygen, the ensuing pause before respiration restarts will be much longer still. In subjects who have trained themselves to this procedure an apnoeic period of ten minutes is by no means impossible.

If we now take one of these subjects towards the end of his period of apnoea and attempt to inflate his lungs with bag and mask as we described previously, we shall find that the actual pattern of respiration can largely be dictated by our efforts. The total volume of respiration, however, still is not controlled by the operator unless altogether excessive pressures are used. If we increase the rate of our attempts to inflate the lungs we shall find that the volume of air that we can put into them decreases so that the total ventilation is determined rather by the subject's muscular activity than by the method or frequency of the artificial operation. This is true also, of course, of a conscious subject who has not hyperventilated if we use force enough to overcome the confusing action of his Hering-Breuer reflex.

When we attempt similar manœuvres of inflation upon a lightly anesthetized patient we shall find ourselves opposed by the Hering-Breuer reflex just as in the conscious man, indeed the irritability, so to speak, may be increased above normal. At slightly deeper planes of anaesthesia we find that we can increase the respiratory excursion each time that the patient inspires and in this way produce passive hyperventilation. Naturally as we are increasing the tidal exchange we shall increase the rate of absorption of the anaesthetic and the speed with which anaesthesia deepens. Thus whether by design, or by inadvertence, the patient will frequently become so deep that neither the nervous mechanism nor the chemical mechanism, whereby total ventilation seems to be limited, will operate. The patient comes into a state when we can do almost anything we wish with his respiration. We can over-ventilate him, we can under-ventilate him, or we can leave him without ventilation at all

carbon tetrachloride. Until spontaneous respiration has commenced, however, carbon-dioxide would appear to have no place in the treatment.

On the other hand the value of administering oxygen during the period of artificial respiration is clear. We have already seen that dogs can be maintained alive in an atmosphere of 100% oxygen, without respiratory movement. It is apparent therefore that if we can administer oxygen it will, so to speak, compensate for deficiencies in our technique of artificial respiration.

The methods of artificial respiration may be classified, briefly, as follows:

- (a) Prone pressure methods.
- (b) Supine pressure methods.
- (c) Postural methods.
- (d) Positive inflation and/or deflation of the lungs, either manually or by means of mechanical devices.
- (e) Methods of artificial respiration which depend upon the application of great stimulus to one or other of the respiratory reflexes.

The efficiency of the various methods has been much debated in the past but unfortunately the subjects used for experiment have nearly always been breathing conscious men or men who have voluntarily breathed themselves into apnœa. We realize now that little information of value can be secured on such subjects.

Few experiments have been carried out upon subjects or patients apnœic from anæsthesia or other cause.

Waters and Bennett [11] amongst others have reported on such experiments.

In 1942 Professor R. R. Macintosh and the staff of the R.A.F. Physiological Laboratory carried out further experiments on these lines using a deeply anæsthetized subject in apnœa believed to be due to deep anæsthesia rather than to acapnia. The respiratory tracings showed that considerably greater inflation of the subject's lungs was possible by pressure than was in fact obtained by most of the manual methods of artificial respiration. Thus the limitation upon ventilation appeared to lie with the methods rather than with the subject. From the records it would appear that either Schaefer's, Silvester's or Eve's, or any other rational method of artificial respiration, provided that it is intelligently carried out and a clear airway is maintained, can produce adequate ventilation of an unconscious apnœic subject. More important than the actual method chosen is the intelligent application of it.

If we may then assume that any method, within reason, will give us the necessary pulmonary ventilation, is there yet another factor to be considered?

In 1943 Cordier [12] drew attention to the possibility that methods of artificial respiration either hinder or assist the circulation. Cordier expected that methods which produced a negative pressure within the thorax, as for example Silvester's, might be expected to assist the circulation. Cordier made measurements on a cadaver and he found that the pressure changes within the ventricles and auricles were greater with a method such as Silvester's than with an intermittent pressure method. Cordier was cautious in interpreting these results and he advocated further experiments on curarized apes. Volpitto [13] and others, Thompson and others [14], have experimented on animals in respiratory and cardiac arrest to see whether artificial ventilation produced blood circulation. In general their results showed that the circulation produced was negligible in these circumstances.

The interval between cardiac arrest and a point when resuscitation by any means is impossible is extremely brief. It is unlikely that we shall often be able to intervene in this very brief interval. Therefore, it is perhaps of more importance to know what a method of artificial respiration can do to the depressed circulation of a subject who has already reached respiratory arrest but is not yet in cardiac arrest. Hemingway and Neill [15] have published observations on dogs under deep anæsthesia with arrested respiration. They first established that when ventilation with a respiration pump was adequate, the maximum oxygen consumption by the animal had been reached. That is to say, further increases in respiration did not increase the oxygen uptake. When they tried artificial respiration by a variety of methods, all producing ventilation above the adequate level, they found that there was a considerable difference in the oxygen consumption depending on the exact methods used. This suggested that a factor other than ventilation was involved and that a particular method might be superior, not only because of the better ventilation it produces, but because of some other effect. Hemingway and Neill suggested that this other factor may be the circulation rate. In most animals with which they experimented they found that while the circulation rate in a deeply anæsthetized subject respired by means of a pump was some 50% below the rate during light anæsthesia, if the same degree of ventilation was produced by a postural method, the cardiac output rose and almost reached the light anæsthesia level.

Clinical trials on fit men breathing under increased pressure of 8 to 15 mm.Hg showed that a proportion of them will, after a few minutes, show some circulatory failure or syncope. The incidence of this faint varied from one investigation to another but was of the order of 5% of individuals.

Animal experiment shows that a maintained positive pressure of 5 mm. of mercury has a variable effect upon the cardiac output, sometimes decreasing it and at other times increasing it. Kahn [5] and others have calculated that at 5 mm. increased pressure the work of ventilation is somewhat reduced. Above this pressure the work involved in respiration is increased. If the positive pressure is higher (about 20 mm.Hg) the venous pressure always increases, the systemic blood-pressure usually falls and the pulmonary blood-pressure rises. The effects are more severe if the chest is closed than if it is open [6, 7, 8, 9].

Carr and Essex [10] report that if dogs are ventilated to a positive pressure of about 15 mm. of mercury intermittently released to about 1.5 mm. of mercury, a certain number developed what they call fatal apnoea. This reaction was absent in vagotomized animals but was not modified by normal doses of atropine. Even small hæmorrhages produced a serious deterioration in the dogs' condition and in those which died there was acute parenchymal and subpleural emphysema. The serious effects were not noted, however, until the increased pressure had been maintained for three hours or more.

Beecher has rightly pointed out that though the effects of increased pressure on experimental animals may not seem to be very serious, they might well be much more significant in sick or injured human subjects. There are grounds for believing that the increased pressure within a closed system may be responsible for deterioration of cardiac output when the pressure has been maintained, during operation, for an hour or more.

In summary, if we allow a patient under anæsthesia to maintain spontaneous respiration of adequate volume, he can, so to speak, protect himself against grave abnormality of blood gases or intrapulmonary pressure changes. If we institute controlled respiration we must realize that we are usurping these important protective functions. The utmost care must then be taken to avoid damage. Generally speaking, unless there is good reason for abandoning it there seems to be a great deal to be said for maintaining spontaneous respiration.

Let us now turn to artificial respiration as used for the resuscitation of subjects who have ceased to breathe in some emergency. First, let us consider one or two points about the nature of our subject.

If a man is subjected to anoxia by being exposed, let us say, to an atmosphere of nitrogen, he will first of all hyperventilate. This hyperventilation may be very considerable, of the order of 30 to 50 litres per minute. Naturally carbon-dioxide is lost and the alveolar pressure of it falls very low. Later the effect of the anoxia will be to depress the respiratory function and respiration will become shallow, irregular and will eventually cease. If arrest occurred very abruptly following the period of increased breathing we might expect the subject to reach respiratory arrest with a low pressure of carbon-dioxide in the blood and the alveoli. On the other hand, if the period of depressed respiration before arrest is prolonged, carbon-dioxide must build up within the subject and he will reach respiratory arrest from anoxia with a high pressure of carbon-dioxide in his blood. In fact, animals asphyxiated with either nitrogen or helium stop breathing with high pressure of carbon-dioxide in the blood. Furthermore, a long period of ventilation at normal rate is needed before the carbon-dioxide level falls to normal.

In the case of subjects who have taken an overdose of a depressive drug there is every reason to expect a high carbon-dioxide level at respiratory arrest and this is found. In the case of drowning or asphyxiation by throttling, carbon-dioxide cannot escape from the body at all, and high pressure of carbon-dioxide in the lungs and blood will occur. In passing it must be mentioned that James and others experimenting on drowned dogs did not confirm this expectation. Their results showing unusually low carbon-dioxide pressures, must be regarded with reserve, I think, until they are further elucidated.

Therefore, in all the cases to whom we shall apply artificial respiration in emergency we may anticipate an existing high pressure of carbon-dioxide in the lungs and blood. There would seem therefore to be no place for the use of carbon-dioxide during the period of artificial respiration.

Once respiration has started spontaneously the state of affairs may be slightly different. If the agent which is causing the trouble is a volatile one which can be excreted through the lungs, then there is something to be said for maintaining a high level of ventilation even though it may be at some cost. For example, in carbon monoxide poisoning the rate at which the carbon monoxide is lost from the system is determined in part by the ventilation volume. In this case we might be willing to accept the fact that we were producing higher carbon-dioxide pressures and nevertheless administer carbon-dioxide for the sake of the increased ventilation. The same might well be true in the case of a volatile agent such as

Section of Obstetrics and Gynæcology

President—A. J. McNAIR, F.R.C.S., F.R.C.O.G.

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DISCUSSION: SOME UROLOGICAL PROBLEMS IN GYNÆCOLOGICAL SURGERY

Mr. Everard Williams: *Vesico-vaginal fistula and the divided ureter*.—When the subject of vesico-vaginal fistula is under consideration the work of Marion Sims (and his successor Emmett) comes first to mind.

The problems that awaited his solution, his early misfortunes and later triumphs are well known.

In 1932 I had the opportunity of observing the work of that master urologist Latzko, of Vienna.

His wards in Elizabeth Hospital were filled with cases of urinary fistulæ, but they had not arisen from neglected confinements in slave labour, they were the sequelæ of gynæcological surgery in other clinics.

The latest figures from the Mayo Clinic reveal that of the cases of vesico-vaginal fistula under treatment 60% were of gynæcological and only 40% of obstetric origin.

The Sims' operation was evolved to deal with a fistula lying low near the urethra, usually of large size and adherent to the symphysis pubis, if adherent at all.

The fistula of gynæcological origin is found near the base of the trigone, is frequently multiple and, if adherent, the adhesion is to the ischial spine. It has an important anatomical relation—the ureter, which may be *involved* in the fistula, and which will assuredly be endangered in the repair. The same applied to many obstetric fistulæ.

Now it has long been known to urological surgeons that the bladder is an organ which takes kindly to surgical trauma. The mucous membrane is vascular and the wall muscular, so that surgical wounds heal readily, provided conditions are right.

In the year 1881, Trendelenburg was able to put into execution a plan of operation in a case of vesico-vaginal fistula that had been in his mind for some time. By means of a suprapubic transvesical approach, he attacked a high-lying vesico-vaginal fistula. As happened in the case of Marion Sims, this first operation proved unsuccessful, but undaunted and convinced of the merit of the operation, he persevered, later cases brought success, and in 1890 he published a case which he had operated on and cured in 1888.

In my modification of the Trendelenburg operation the patient is suitably anæsthetized and placed in the Trendelenburg position. The vagina is packed with gauze and a small volume of fluid is introduced into the bladder. The abdominal wall is divided in the mid-line. The bladder is exposed without opening the peritoneal cavity.

Stay sutures are passed through the bladder wall on either side of the mid-line and the bladder opened longitudinally. The necessary inspection is made and the diagnosis confirmed. A self-retaining bladder retractor with interior illumination, such as a Clifford Morson's, is introduced. The only other special instruments required are an angled knife of small size, like a cleft palate knife, two sharp hooks mounted on long handles, and a suction apparatus.

On the side on which the fistula lies, a ureteric catheter is passed into the ureter and its integrity established. This is left in situ throughout the operation.

TABLE I

Method	Rate/min.	Vol. of inspired air/min. c.c.	Oxygen consumption c.c.
Silvester	13	4,180	104
Schaefer	14.6	4,360	149
Eve	9	4,970	210

As yet no direct measurements of cardiac output have been made upon man during artificial respiration. It is possible, however, that similar variations to those noted by Hemingway and Neill do exist. Professor Macintosh, again working with the staff of the R.A.F. Physiological Laboratory, made measurements of the oxygen consumption of a man reduced to respiratory arrest by means of curare. The results are set out in Table I and it will be seen that although the ventilation with each of the three methods was similar, the oxygen consumption varied greatly from one method to another. It certainly suggests that ventilation should not be the only criterion in choosing a method of artificial respiration.

In advising upon a method of artificial respiration for emergency use, therefore, we shall first of all insist upon intelligent, efficient observation of the patient. The maintenance of a clear airway is of paramount importance. In some cases, where the personnel are not well trained, it may be better to use a method which will work fairly well provided that the textbook instructions are followed, rather than one which may potentially be better but which may require more intelligence and discretion in its achievement. As an example we might cite mouth-to-mouth respiration. There is no doubt of the efficiency of this method and it appears simple. Nevertheless intelligent observation of the patient is not easy, nor is it easy to maintain an adequate airway. The method is simple in that it requires no apparatus and it can be carried out in very confined spaces but it seems probable that considerable discretion is required if it is to be efficient.

We shall probably conclude that on the matter of ventilation it does not matter a great deal which of the standard methods we choose.

On the matter of circulation we shall probably conclude that matters are not quite so even. The variation in oxygen uptake between equal ventilation with different methods does suggest that they have varied effects upon the circulation. Final proof of this is not yet available.

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Dr. W. O. Moore Ede enquired of Dr. Pask whether, provided he was fully oxygenated, he would prefer to be over- or under-ventilated, if he were anesthetized.

Dr. R. P. Harbord agreed with Dr. Pask's statement about the patient's condition during "controlled respiration", but thought it preferable to assess it after removing the mask (*Proc. R. Soc. Med.*, 1947, 40, 174). He felt that pulmonary ventilation was loosely judged by nitrous-oxide-oxygen standards instead of those of normal conscious subjects. Because it is difficult to estimate tidal volume by the visible alterations in spherical bags of varying capacity and content, he uses a test bag of 600 c.c. capacity—by-passed from the bag connected to a Water's absorber—as a guide in estimating the adequacy of tidal volume.

Dr. E. A. Pask, in reply to Dr. W. O. Moore Ede, said that if gross under-ventilation approaching standstill was contemplated then he would certainly prefer to take the risks of over-ventilation. It was not at present possible to assess the relative disadvantages of lesser degrees of over- and under-ventilation.

(2) *Good light*.—Except in the case of low-lying vesico-vaginal fistulæ, the surgeon can better visualize the important step in the operation, viz. the repair of the bladder wall; the repair of the vaginal wall is of small moment.

(3) *Combined fistulæ* (in the repair of).—When there is both vesical and ureteric injury, an abdominal approach is clearly essential. Both lesions can be repaired in one operative field and in one operation.

(4) *Failed vaginal operation*.—In surgical literature, cases are recorded of success with Trendelenburg's operation, after eleven successive failures with the Sims' operation.

(5) The abdominal operation is of much shorter duration than the vaginal operation.

Indications for the Trendelenburg operation: (1) All vesico-vaginal fistulæ of gynæcological origin. (2) High-lying fistulæ of obstetric origin, because of the proximity of the ureter. (3) Obstetric fistulæ, with adhesion to the ischial spine. (4) Failure, or recurrence after the Sims' operation. (5) Combined uretero-vaginal and vesico-vaginal fistulæ.

Miss Catherine Lewis: *Fistulæ of the bladder*.—Operation injuries, radium burns, fistulæ caused by malignant disease, and those due to rupture of a pelvic abscess. The majority of these fistulæ open into the vagina.

With regard to operation injuries, one type may be considered very briefly. I allude to cases where the patient has not been catheterized and there is a consequent risk of damage to the bladder while the abdominal incision is being made.

An injury to the peritoneal surface is not likely either. The peritoneum is closely attached to the postero-superior surface of the bladder over a small area only about the size of half a crown, and it is not likely to be compromised in the course of a gynæcological operation.

A much more likely accident is that the bladder may be injured while it is being separated from the cervix and the anterior vaginal fornix in the course of a panhysterectomy or even of a subtotal removal of the uterus. This part of the operation is often very difficult where the tissue planes are masked by malignant growth, where there is a marked degree of old inflammation with dense adhesions, or if simple tumours, fibroids or cysts have distorted the normal anatomy of the region. It is quite possible to make very large vesical wounds in such circumstances, but these are actually less dangerous than small ones as it is not likely that they would be overlooked at the time. Apart from a direct injury, the bladder wall may be so thinned during the process of stripping it from the vagina that sloughing will occur later, after the lapse of several days, when an ominous leak begins. In all these accidents the fistula usually opens into the vagina from the base or the trigone of the bladder.

There is another gynæcological operation in which the bladder is particularly vulnerable—that of plastic repair to the anterior vaginal wall. The two organs are intimately connected for a length of about two and a half inches, as is clearly demonstrated in the operation for total cystectomy, and it is not always so easy to separate them by blunt dissection; numerous small vessels and strands of fascia have to be cut deliberately. The bladder wall may thus be snipped, and the resulting wound is low on the base or on the trigone. It must always be borne in mind that, in any of these operation accidents, the damage may not be confined to the bladder but that one or both ureters may be involved. I believe that some surgeons appreciate the risk so much that they make a practice of inserting ureteric catheters prior to undertaking a difficult pelvic or perineal operation.

Fistulæ due to radium burns are still seen occasionally though, fortunately, they are rare. They follow radium insertion into the vagina for treatment of cervical carcinoma if a pack slips and the bladder is insufficiently protected from the irradiation. This may only result in comparatively minor damage such as mucosal ulceration, though this can be troublesome enough, but, if sloughing occurs, it may be extensive and finish as a vesico-vaginal fistula surrounded by devitalized and fragile tissues.

Malignant growths of the uterus or vagina tend to infiltrate the bladder and eventually to make an opening, either vesico-cervical or vesico-vaginal, which, naturally, goes on increasing in size. In this connexion it might be thought advisable, before treating an advanced condition, to make a cystoscopic examination in order to exclude vesical involvement. In an early stage this shows itself as a localized area of hyperæmia and possibly a little wrinkling suggestive of fixation, later a projecting mass with obvious signs of infiltration.

A pelvic abscess sometimes ruptures into the bladder and though, after a vesical crisis, its contents can be mainly discharged in this way, complicated fistulæ have been known to occur, opening on to the abdominal wall, into the vagina, or both.

The *symptoms*, once a fistula is established, are unmistakable—there is a constant leak of urine. The only difference between one case and another is that, in some patients, normal micturition goes on as well, whereas in others the whole of the urine runs away uncontrollably.

Assuming the fistula not to involve the ureter, a free dissection is made between the bladder wall and the vagina until healthy tissue is reached, all scar tissue is excised and the edges of the wound trimmed, while keeping it in *tension* with the sharp hooks and dry with the suction nozzle.

The vaginal wall is then closed with two mattress sutures tied from the vaginal side.

The fistula in the bladder is closed with interrupted sutures of fine non-chromic catgut, passed through mucous membrane and muscle wall. The bladder itself is not closed but sutured around a wide rubber tube. (A smaller size than a Marion tube is used.)

The abdominal wall is closed in layers in the usual way. There is no resort to catheterization. The rubber tube is changed on the fifth day and removed on the eighth day.

During the first three days, frequent bladder irrigation is carried out, say every three or four hours, through the abdominal tube, otherwise there is no special treatment.

Investigation of a case.—Towards the end of the first week after an extirpation of the pelvic organs, it may be found that the patient is no longer dry: that a fistula exists is all too apparent.

The immediate treatment usually advised is conservative, in the hope that spontaneous healing will occur. I doubt the wisdom of this course and think it is better to perform a cystoscopy at once and unless the fistula is of the smallest size proceed to perform suprapubic cystotomy and sew in a Marion tube and keep the bladder empty and at rest.

It may be argued that this may be unnecessary, because spontaneous healing may have occurred and the operation need never have been performed, but while the truth of this cannot be denied, it is my submission that it is looking at the problem from the wrong angle. A more difficult and hazardous operation at a later date may be averted, if this simple step is taken at once.

Presented with a case at a later date, the first point for decision is, when to conduct the repair. The practice of different surgeons varies in this particular, with recommendations to wait for the occurrence of spontaneous healing up to a year.

Once the track of the fistula is epithelialized, it will never heal and if it is not epithelialized it will have closed in a matter of weeks. The life of these patients is very miserable while the fistula is present, and unless it is of almost microscopic size, I cannot see any advantage to be gained in waiting longer than six weeks from the time of healing of the primary wound.

The preliminary investigations include a bacteriological examination, with appropriate chemotherapy if infection is present; intravenous pyelography and cystoscopy with ureteric catheterization on both sides. The latter step is, I believe, the only sure way of determining the presence or absence of a ureteric lesion.

A combination of uretero-vaginal and vesico-vaginal fistula may well be present and the excretion urography may show an apparently intact ureter, for with a large vesico-vaginal fistula there may be a retroperitoneal pool of dye and this may obscure the ureteric lesion, or the diagnosis may be incorrect.

In the presence of a ureteric fistula the Trendelenburg operation does not suffice and the operation must be transperitoneal for the repair of the ureter combined with transvesical closure of the vesical fistula—but the operation in general principles is the same. The vesical fistula is closed before the damaged ureter is dealt with.

The divided ureter.—Solution of continuity of the ureter may result from its division by the surgeon's knife, inclusion in a ligature, or necrosis of the wall through interference with the blood supply.

The first only of these happenings is apparent during the course of an operation; it may be deliberate as when the ureter runs through carcinomatous infiltration found to be more extensive as the operation develops than was anticipated when it began. The correct treatment in such circumstances is, I believe, to perform uretero-vesical anastomosis after mobilizing the bladder if need be, or failing this, as a second best, to perform uretero-colonic anastomosis. If, however, the ureter is accidentally divided, should the attempt be made to suture together the divided ends and perform anastomosis in that way? Textbooks of operative surgery suggest that this should be done, but I believe this view is wrong, because of the subsequent development of hydronephrosis. It is my submission that the accidentally divided ureter should be treated in a similar manner to that of the deliberately divided ureter by implantation into the bladder or colon, as the circumstances of the case dictate.

In pelvic surgery the ureter is in danger at two particular sites, viz. at the pelvic brim and near the ischial spine, in the latter location suture of the divided ends would be technically almost an impossibility.

The Trendelenburg operation has the following advantages:—

(1) *Good access.*—Anyone familiar with both routes knows that far better access is obtained with the transvesical than with the vaginal approach. This applies to a fistula in any part of the bladder.

such a case is probable—a two-stage operation is best; first an abdominal section and reimplantation of the ureter into the bladder and, later, repair of the vesical defect from the vaginal aspect. It may sometimes be possible, when the bladder is opened for the reimplantation, to repair the fistula from inside and it is, of course, most satisfactory to all concerned if this can be done, but it is not worth trying unless the chance of success is really good. As I said before, I have no experience of both ureters leaking into such a fistula, but should suppose that two if not three repair operations would be required. I believe it would be difficult to repair both bladder and ureter from the vagina, and should be glad to hear the experience of others in such cases.

Fistulae resulting from radium burns are very difficult to deal with. They are generally larger than operation wounds and the tissues are so devitalized as to have almost no healing capacity, so that even the most careful repair may break down. I am rather inclined to think that it is wise not to attempt to close the hole completely at one sitting, at all events if it is a large one, such as the size of a halfpenny, but to plan for two operations and try to make sure of a portion of success at each stage. If, in spite of everything, the fistula keeps on breaking down, it would seem best to abandon the attempt and to transplant the ureters into the colon.

There is nothing to be done locally where the tissues have been eaten away by malignant disease, and generally it is best to provide a portable urinal and leave events to take their course. But for a woman a portable urinal is very uncomfortable and difficult to adjust—it is almost necessary to design a new one for each patient—and in an occasional case ureteric transplantation might be considered as a palliative measure if the patient's general condition, renal function, and probable length of life would seem to warrant it. But it is such a serious operation, much more so than a palliative colostomy for instance, that the cases where it is justifiable are likely to be rare.

I do not think any definite suggestions can be made as to the treatment of a fistula originating in a pelvic abscess. Some of them are acute and some tuberculous, and the manifestations are too varied. Each case must be considered separately. The only rule, and this applies to any vesical fistula, is that the bladder must be thoroughly mobilized and firmly repaired, if the patient is to lead a comfortable life.

Mr. R. Ogier Ward suggested that he might usefully indicate in what manner a urologist could be of assistance in such cases. He alluded first to the treatment of very severe degrees of vesico-vaginal fistula of obstetric origin, such as were met with in native women. These were often so extensive that the anterior vaginal wall was absent and in its place only vesical mucosa was visible, and often the urethra itself was destroyed. In such cases he had seen the excellent results achieved by the surgeons in Nairobi where women came from the native reserves continuously—a testimony to success—for implantation of the ureters into the colon. None the less surgeons should not be too eager to perform this operation for which, it should be remembered, a healthy rectum with an undamaged sphincter was essential. Every means to effect local repair should first be tried, for transplantation was a severe procedure and a long term follow-up would show that some patients did not escape serious and perhaps fatal effects after a lapse of many months. In commoner and less severe cases of fistula certain preliminary examinations were important, particularly excretion urography, which would bring to light any ureter damage which might be present. If the vagina was packed with gauze and a flushing cystoscope used, the extent of the fistula and the state of the bladder could usually be accurately determined. Should a combined operation through bladder and vagina be proposed it was important to use a proper bladder retractor and to arrange for good illumination. The vesical mucosa must always be well freed from the scar at the site of the fistula and mobilized so that it could be closed without tension. This was the most important step in the operation and if it was well done the repair of the vaginal wall was merely a reinforcement of it, which, however, should not be omitted. He mentioned Swift Joly's operation which would be found useful in severe degrees of fistula. The peritoneum was opened, the apex of the bladder defined and the cavity opened just anterior to this; the incision through the bladder wall was then extended down to and around the fistula, the vagina being separated during the dissection. Stitches were then inserted to pick up the angles between the two organs, when tied these sutures had the effect of inverting the walls of each organ into its own cavity, other sutures being added to close the edges. In this, as in the direct bladder approach to the fistula already mentioned, it was better to maintain cystotomy drainage for a fortnight rather than to rely upon an indwelling catheter.

Mr. Ogier Ward, in reply to questions, said he had no experience of the operation of closure of the vagina so that the cavity became part of the bladder. When ureters were to be transplanted excretion urography was essential, this would often reveal duplication of the

This depends on the size of the opening; if it is a small one the escape does not keep pace with the renal output, and the normal function is retained though the patient is always wet. Often the position of the defect is indicated by an indurated area in the vaginal vault, though this may be masked by the scarring of a recent operation. This question of a partial or a total leak is very important to the surgeon as, in the first case, but not the second, the position and general lay-out of the fistula can be seen through a cystoscope and treatment planned accordingly.

Treatment.—Any injury to the bladder detected during the course of an operation should be repaired at once. The healthy bladder is a good healing organ, and the size of the opening does not matter, provided that it is mended immediately and well, and the bladder kept empty by drainage. Two layers of plain catgut sutures are used, and a self-retaining catheter inserted. Unless the wound is very extensive suprapubic drainage is not necessary. An indwelling catheter is certainly very uncomfortable to the patient, and some surgeons object to using one. It is apt to irritate the urethra and to cause vesical spasms but it is preferable to a suprapubic drain and the subsequent fixation which it entails. The catheter is kept in position for seven to ten days and, during that time, belladonna in some form may be given. Some operators prefer a suction apparatus to make even more sure of preventing tension.

If, however, the accident is unobserved at the time and if a small leak develops later (this occurs almost at once in the case of a direct injury, or in from five to ten days where necrosis supervenes), an indwelling catheter should be inserted at once, after which the wound may heal of itself. But, if a fistula once becomes established or if the original repair breaks down, a formal operation must be undertaken, and the only questions are—when to do it and what is the best method of approach. In the early days of its existence the edges of a vesico-vaginal fistula are ragged and friable and, especially if the opening is a small one and the drainage not very free, phosphatic concretions tend to form in and around it, and the escaping urine is thick and offensive. It is useless to attempt a repair at this stage; cleaning-up must be done first. Concretions, if present, are extracted from the vagina, and douches and urinary antiseptics given until all sepsis has disappeared and the edges of the defect are clean and well healed, probably in not less than three weeks' time. It is true that a good deal of scar tissue may form in the meantime, but this cannot be helped; at least there is a clean field to work in. On the other hand, operation should not be unduly postponed for fear of contracture of the bladder, not so much with small fistulae but certainly where there is a total leak. I remember a case where a fistula of two years' standing was cured but the patient, far from being grateful, complained that her bladder always felt full. 'And, indeed, it' had a smaller capacity than normal.

With regard to the method of approach this, to my mind, depends on the position of the opening in the bladder. If it is on the back wall but well above the trigone I like to close it from inside the bladder, but, if it is very low on the base, in the interureteric region or involving the trigone, I think a vaginal approach is best. This is my general rule, but complicated fistulae, possibly involving one or both ureters, must be considered individually according to the case. Simple operation fistulae are not likely to be adherent to bone. There is also the transperitoneal method described by Legueu, in which the peritoneal fold reflected from the back wall of the bladder across the vaginal vault is incised in the mid-line and the two organs dissected apart until the respective openings and the surrounding tissues are completely isolated from each other and the holes mended. This last point is of the utmost importance, whichever method of approach is chosen. There must be free undercutting and separation of the two organs, otherwise the repair will break down. Subsequent to the operation the bladder must be kept from filling for several days.

If one or both ureters are involved in the fistula it may be very difficult to diagnose the extent of the damage. I have never seen both ureters leaking into a vesico-vaginal fistula though I have known both to be divided during a difficult hysterectomy. With a large vesical defect it is impossible to fill the bladder for a cystoscopic examination, or, at any rate, for one which will give a clear view and permit of ureteric catheterization. It is obvious that the hole is there, and indeed sometimes a finger in the vagina passes through it, but one may not be able to make out the exact position or extent of the damage. In this case an X-ray—namely, an excretion pyelogram—is extremely helpful. If a ureter, perhaps slightly dilated, retains the dye an injury to it must be suspected. In cases where a routine cystoscopy is possible and the fistula, even though very small, lies anywhere near one of the ureteric orifices, that ureter should be catheterized. A catheter will not pass the site of injury, and a dye given intravenously does not appear from that side.

The treatment of a vesico-uretero-vaginal fistula must be planned according to the merits of each case. I am inclined to think that, if the vesical opening is at a low level—which in

such a case is probable—a two-stage operation is best; first an abdominal section and reimplantation of the ureter into the bladder and, later, repair of the vesical defect from the vaginal aspect. It may sometimes be possible, when the bladder is opened for the reimplantation, to repair the fistula from inside and it is, of course, most satisfactory to all concerned if this can be done, but it is not worth trying unless the chance of success is really good. As I said before, I have no experience of both ureters leaking into such a fistula, but should suppose that two if not three repair operations would be required. I believe it would be difficult to repair both bladder and ureter from the vagina, and should be glad to hear the experience of others in such cases.

Fistulae resulting from radium burns are very difficult to deal with. They are generally larger than operation wounds and the tissues are so devitalized as to have almost no healing capacity, so that even the most careful repair may break down. I am rather inclined to think that it is wise not to attempt to close the hole completely at one sitting, at all events if it is a large one, such as the size of a halfpenny, but to plan for two operations and try to make sure of a portion of success at each stage. If, in spite of everything, the fistula keeps on breaking down, it would seem best to abandon the attempt and to transplant the ureters into the colon.

There is nothing to be done locally where the tissues have been eaten away by malignant disease, and generally it is best to provide a portable urinal and leave events to take their course. But for a woman a portable urinal is very uncomfortable and difficult to adjust—it is almost necessary to design a new one for each patient—and in an occasional case ureteric transplantation might be considered as a palliative measure if the patient's general condition, renal function, and probable length of life would seem to warrant it. But it is such a serious operation, much more so than a palliative colostomy for instance, that the cases where it is justifiable are likely to be rare.

I do not think any definite suggestions can be made as to the treatment of a fistula originating in a pelvic abscess. Some of them are acute and some tuberculous, and the manifestations are too varied. Each case must be considered separately. The only rule, and this applies to any vesical fistula, is that the bladder must be thoroughly mobilized and firmly repaired, if the patient is to lead a comfortable life.

Mr. R. Ogier Ward suggested that he might usefully indicate in what manner a urologist could be of assistance in such cases. He alluded first to the treatment of very severe degrees of vesico-vaginal fistula of obstetric origin, such as were met with in native women. These were often so extensive that the anterior vaginal wall was absent and in its place only vesical mucosa was visible, and often the urethra itself was destroyed. In such cases he had seen the excellent results achieved by the surgeons in Nairobi where women came from the native reserves continuously—a testimony to success—for implantation of the ureters into the colon. None the less surgeons should not be too eager to perform this operation for which, it should be remembered, a healthy rectum with an undamaged sphincter was essential. Every means to effect local repair should first be tried, for transplantation was a severe procedure and a long term follow-up would show that some patients did not escape serious and perhaps fatal effects after a lapse of many months. In commoner and less severe cases of fistula certain preliminary examinations were important, particularly excretion urography, which would bring to light any ureter damage which might be present. If the vagina was packed with gauze and a flushing cystoscope used, the extent of the fistula and the state of the bladder could usually be accurately determined. Should a combined operation through bladder and vagina be proposed it was important to use a proper bladder retractor and to arrange for good illumination. The vesical mucosa must always be well freed from the scar at the site of the fistula and mobilized so that it could be closed without tension. This was the most important step in the operation and if it was well done the repair of the vaginal wall was merely a reinforcement of it, which, however, should not be omitted. He mentioned Swift Joly's operation which would be found useful in severe degrees of fistula. The peritoneum was opened, the apex of the bladder defined and the cavity opened just anterior to this; the incision through the bladder wall was then extended down to and around the fistula, the vagina being separated during the dissection. Stitches were then inserted to pick up the angles between the two organs, when tied these sutures had the effect of inverting the walls of each organ into its own cavity, other sutures being added to close the edges. In this, as in the direct bladder approach to the fistula already mentioned, it was better to maintain cystostomy drainage for a fortnight rather than to rely upon an indwelling catheter.

Mr. Ogier Ward, in reply to questions, said he had no experience of the operation of closure of the vagina so that the cavity became part of the bladder. When ureters were to be transplanted excretion urography was essential, this would often reveal duplication of the

ureter if it existed, even so this was a complication for which the surgeon must be on guard when actually operating. He had always supposed that the Sims' operation was unquestionably the best treatment for the usual case of vesico-vaginal fistula of obstetric origin such as was met with in civilized countries, but the combined bladder and vaginal method had an important place in cases of high fistula such as occasionally followed gynaecological operations, and also when operation by the vaginal route alone had been unsuccessful.

Professor G. Grey Turner: As Mr. Everard Williams has said we cannot allow ourselves to approach this subject without thinking of Marion Sims if only in admiration of his marvellous courage and perseverance. Let us always remember the primitive conditions of his environment and recall that he had to operate again and again on those brave women without the inestimable boon of anaesthesia.

The discovery of how to expose the parts concerned in the management of vesico-vaginal fistula by the adoption of the position which will be coupled with his name in perpetuity is enough to command our lasting gratitude. May I remind members that the story was delightfully retold by Professor Chassar Moir (1940, *Brit. med. J.* (ii), 773).

Of course since the time of Sims there have been many pioneers who have made notable contributions to the subject and I just want to recall to the Section that it was my old teacher, Professor Rutherford Morison, who first insisted on the importance of recognizing that the parts involved—the bladder and the vagina—must be separated from one another and individually repaired if interference is to have a reasonable chance of success (*Northumberland and Durham Medical Journal*, 1895, No. 213).

I wonder if in this audience I dare mention the early treatment of vesico-vaginal communications especially in obstetric cases, realizing that these are now quite rare in this country, and that in those parts of the world where they still occur with lamentable frequency, the patients are seldom seen until the fistulous track is well established. The parts involved have a very good blood supply and a great capacity for healing if they can only be kept clean and the urine diverted before the formation of cicatricial tissue binds the parts together and stabilizes the fistulous track. To attain these objects vaginal drainage should be promoted by raising the head end of the bed and by douches, fully realizing that it is not the composition of some wonderful douche that matters but the mechanical cleansing which it promotes. The urine should be diverted by catheter drainage via the urethra and by getting the patient to lie as much as possible in the face-down position. I trust that obstetricians will not condemn these suggestions out of hand but will try them.

In the prevention of surgical accidents to the ureter may I stress the importance of actually seeing that structure during a pelvic laparotomy by deliberately exposing it so that it can be gently thrust aside with the finger out of harm's way.

I have had a not inconsiderable experience of exposing the ureter over considerable lengths and I know how amenable that structure is to gentle handling.

The investigation and exact diagnosis of these fistula cases have been properly stressed and I would like to extol the value of milk as a bladder injection for demonstrating the site of the vaginal orifice of the fistula; it is better than a solution of methylene blue. A late ureteric fistula, one developing some days after surgical intervention, is probably the result of an area of necrosis which gives way and will probably be a lateral hole. Some of these will heal if a ureteric catheter can be slipped up beyond the opening and left in situ for some days. Meanwhile suction drainage from the site of the fistula will help.

Though those who have tried the method must be impressed with the value of the transvesical operation we should not allow ourselves to be blind to the wonderful success of the vaginal operation in careful and competent hands.

Of course the site of the fistula has a bearing on the choice of route and in those that are high lying the transvesical operation should be the method of election. In this field success is not due to luck but to the application of surgical principles with intelligence. I have often been asked what could be done when a ureter is inadvertently divided in some deep pelvic operation, not necessarily of a gynaecological nature. If both ends can be found and can be approximated without tension they should be directly united by suture and with very good prospect of success.

But it should be end-to-end union and the open ends of the ureters should be enlarged by being trimmed obliquely and then united by a few, not more than four or five, interrupted sutures of very fine absorbable suture material lightly tied. Any effort to make a close watertight union by a continuous circular suture is doomed to failure and will only result in stricture. Free unimpeded drainage by tube conducted to the surface by the most direct route is, of course, essential. If a ureteric catheter can be passed beyond the union it may be a help in

healing but I believe that its use should be reserved for cases where leakage persists for say more than ten days. The external drain should be removed in a week for by that time a track to the surface will be safely walled-off from the surrounding tissues and its contraction may assist in healing.

If easy apposition of the ends is not possible then implantation into the bladder is sound practice provided that it can be done low down so that the ureter in its new course can be kept extraperitoneal. If neither of these methods is possible two rational courses remain. First there is implantation into the large bowel which has proved wonderfully successful though it is not ideal, for some cases do develop an ascending infection which may seriously damage the kidney. (But how encouraging it was to hear a day or two ago from one patient whose ureters were transplanted nearly thirty-four years and another twenty-two years ago. Both are well, the first the mother of three children all born since the transplantation and the second recently happily married.)

The other plan is to bring the upper cut end on to the skin surface by the shortest route so that the problem of the resulting fistula can be deliberately tackled at some later appropriate time and probably by secondary bowel implantation. In any case the lower cut end can be safely left to take care of itself for its open lumen does not appear to cause mischief. Though it has sometimes been advised in the past, I would not now recommend that a divided ureter should be ligatured and allowed to retract into the retroperitoneal tissue though I can confirm that this has often been done without untoward result immediate or remote.

Some cases of ureteric fistula defeat the surgeon and just before leaving the Postgraduate School I had to carry out nephrectomy as the only possible method of dealing with a persistent fistula on to the surface. In that case the circumstances were so unusual as not likely to be met with in the lifetime of most surgeons.

Mr. C. Scott Russell: *Partial colpocleisis for the repair of the vesico-vaginal fistula following successful treatment of cervical carcinoma with radium.*—In the case described the fistula developed as a later sequel to radium treatment for cancer of the cervix. The fibrous avascular quality of the tissue surrounding the fistula made direct closure impracticable. A half-inch cuff of the vaginal wall below the fistulous opening was removed and the vagina closed with silver wire sutures. Continuous bladder drainage was instituted for ten days. After three weeks' time, during which there was no escape of urine, the sutures were removed. Unfortunately the retraction necessary to expose the last suture resulted in a partial breakdown of the repair; this was treated with temporary success by further bladder drainage. A tiny opening remains which it is hoped can be closed by a similar procedure.

Important points in the treatment of such cases:

- (1) Excision of the vaginal cuff at a level below that of devitalized avascular tissues, and the closure of the vagina without tension.
- (2) Continuous bladder drainage for ten to fourteen days.
- (3) The removal of the sutures with great care and gentleness.
- (4) No vaginal examination or coitus for three months.

Professor J. Chassar Moir said that every surgical technique capable of closing a vesico-vaginal fistula merited careful consideration. Naturally, the genito-urinary surgeon with his experience of bladder work felt more "at home" in approaching the lesion from above, while the gynaecologist felt surer of himself in approaching it from below. Nevertheless, it was obvious that if there was a choice of method, that procedure should be selected which would be least drastic or dangerous for the patient. Judged by this standard, the vaginal operation (based on Sims' technique) merited first consideration. To recommend the suprapubic approach for all fistulae (other than those low in the vagina) sounded to him like proposing to perform all tonsillectomies by a dissection through the side of the neck. He disagreed with the statement that high fistulae could not be satisfactorily dealt with from below. By suitable positioning of the patient, by use of suitable retractors and, when necessary, by aid of a generous episiotomy, adequate access could almost always be obtained. In some 50 vesico-vaginal fistula cases, gathered from different parts of the country, he had found that high fistulae (including those resulting from total hysterectomy or the Wertheim operation) had, in general, caused less trouble than certain types of low fistulae involving the vesico-urethral junction. Most of his cases had had many previous operations, including operations by the transvesical route. In spite of this, it had been possible to close the fistula by a vaginal operation. Strict attention had to be given to certain points of technique which the speaker then described with the help of lantern illustrations (*Edinburgh Medical Journal*, 1947, 54, 368).

Mr. V. B. Green-Armytage said that some years ago he had published in the *British Journal of Surgery* (1932) a series of vesico-vaginal fistulae treated by transplantation which were absolutely inoperable from below owing to their size and the fixity of their edges to the surroundings. These cases were seen in India and he was interested to hear Mr. Ogier Ward refer to similar ones that he had seen in Nairobi, for operators in this country had no idea what the young man in the Colonies or in the missionary field had to tackle in the way of obstetric fistulae. Therefore it was imperative before they went abroad that they should see urologists of note doing the colonic transplantation of ureters, for they might be faced by one of these inoperable huge obstetric fistulae almost on their arrival, and so should be able to tackle one *secundum artem*.

Sometimes on opening the abdomen it might be found quite impossible to do a ureteric transplant because of massive old pelvic inflammation and parametritis. The speaker had found this on occasions and could not elevate the ureter without grave danger of complete sloughing or tearing. In such a case might he put in a claim for colpocleisis, that is turning the vagina into the bladder by plastic closure of its introitus. This was not a difficult procedure and provided the patients could be seen now and then during the years, to be sure that no phosphatic stones were forming, they did well. He had found it wise to nurse these patients on the face or in full Sims' position with an indwelling self-retaining catheter for twelve days. The introital scar area was sprayed with acriflavine 1 : 1,000 alcohol solution four times a day and no external strong-smelling dressing allowed.

REFERENCE

GREEN-ARMYTAGE, V. B. (1932) *Brit. J. Surg.* 20, 130.

CORRIGENDUM

Joint Discussion No. 3, Section of Obstetrics and Gynaecology with Section of Radiology, *Proceedings of the Royal Society of Medicine*, 40, 907, December 1947,

DISCUSSION ON SOME ASPECTS OF SURGICAL AND RADIOLOGICAL TREATMENT OF CARCINOMA OF THE CERVIX

The following communication has been received from Dr. G. E. Richards, Toronto, as a correction to his paper "The Radiological Treatment of Carcinoma of the Cervix Uteri", p. 911:

"In my presentation of the results of the radiological treatment of carcinoma of the cervix uteri, figures were used for the purpose of comparing the effectiveness of modern radiotherapeutic methods with those of surgery. The figures used included those of Mr. Victor Bonney, in the compilation of which an error was made, which I hasten to correct, both in fairness to Mr. Bonney and in the interest of a strictly accurate comparison. The corrected figures are as follows:

"Bonney operated upon 500 cases selected out of a total of 800 diagnosed as cervical cancer, i.e. an operability rate of 62.5%.

"Of the 500 cases operated upon, lymph nodes were found *not* involved by cancer in 300 (60%), while in 200 (40%) lymph nodes were involved by cancer.

"Of the *gland-free* cases 159 patients survived five years, i.e. *gross* survival rate 53%. Deducting those lost to follow-up or died of extraneous disease, net survival rate 58%.

"Of the *gland-involved* cases 42 survived five years, i.e. *gross* survival rate 22%; net survival rate 23%.

"The figure 40%, quoted in my paper, was the over-all five-year survival rate and referred to all cases operated upon, not as stated, to Stages I and II only."

Section of Laryngology

President—A. J. WRIGHT

[November 7, 1947]

Snoring

By IAN G. ROBIN

THIS short paper is a plea for the more serious consideration of a complaint which is often a distressing physical and mental handicap. It may ruin a happy marriage, and in some parts of the U.S.A. it is considered justification for divorce. Up to date it has been treated as a comic pastime, and the unfortunate adult sufferers (and even more the agonized relations and associates) have to bear with it in fear of ridicule.

There is almost no world literature on the subject except for the Japanese observers who have devoted some time to it. But we can gain some useful information on the matter from recent work by anatomists and orthodontists who have been studying the mechanism of palatoglossal movements and their relationship to mouth breathing. I am indebted to Dr. J. Whillis, Mr. Gwynne Evans and Mr. A. Nove for most helpful personal conversations.

Definition.—Noisy respiration during sleep may be produced during inspiration and expiration by various structures in the respiratory tract. I propose to limit snoring to sounds made by vibrations in the soft palate and posterior faucial pillars during sleep. This definition excludes sounds made by laryngeal structures including the epiglottis, by the tongue, cheeks, lips or nostrils. Snoring is usually produced during inspiration through the mouth. Sometimes, however, breathing is through the nose (Negus says this occurs in some "gifted individuals"). A short inspiratory snore through the nose with the mouth open may be called a "snort" and some persons are addicted to a series of snorts.

Snoring is involuntary: it stops as soon as consciousness is regained.

Mechanism.—Whillis has shown very clearly by means of a pharyngoscope that the vibrating part in a snore is the thin edge or velum of the posterior faucial pillars. He proved that a reservoir of air is necessary in the nasopharynx: if this space is completely filled the velum cannot vibrate. He also demonstrated that the velum is set in vibration during respiration (usually inspiration) when a "critical point" or position is reached in the relative position of the tongue and soft palate. But not only is it *position* that influences the vibrating parts, it is the *texture* of the velum, and this depends on the tone of the musculature of the glossopharyngeal arch, and the thickness of the tissues (especially the mucosa). The actual pitch of the sound is determined by the so-called "flutter-ratio" of the faucial pillars: Strauss likens the physics to a fluttering flag in a wind—any increase in the force of air intensifies the noise but does not change the pitch. This depends on the density, elasticity, and size of the vibrating part.

Position of the soft palate.—When sucking, the infant's soft palate is in close apposition to the back of the tongue (fluid being squirted intermittently back into the pharynx). A suckling is therefore unlikely to snore during sleep, as the relation between tongue and soft palate is unlikely to change. When the chewing habit develops the soft palate is raised away from the tongue. If mouth breathing occurs for any reason, the palate is free to vibrate. In adults the position is regulated by the tone of the muscles as well as the amount of airway in the nose. Nove maintains that a short ramus of the mandible makes the palate lie away from the dorsum of the tongue.

Position of the tongue.—This plays some part in determining the "critical point". If during mouth breathing the dorsum is arched, or falls back, then it will be near to the velum of the fauces. The position of the head may govern that of the tongue. Sleeping on one's back is considered a common cause of snoring, because the tongue falls back more readily. The act of swallowing (the mechanism of which is so admirably described by Negus, 1942, *Proc. R. Soc. Med.*, 36, 85) actually inhibits that of snoring; there may be complete cessation or resumption, depending on whether the tongue returns to the snoring or "critical" position, and also whether the reflexes to be described are inhibited.

With regard to the position of the tongue there seems to be no influence from the presence or absence of teeth or dentures in the production of snoring. On the other hand an orthodontic "monoblock" or "Andresen" splint can mould the dental alveolar pattern (probably without changing the basal bone one) and so lead to less mouth breathing.

Tone of the glossopharyngeal musculature.—This has a governing role for the "critical point", as it decides the positioning and elasticity of the parts. Gwynne Evans and Whillis agree that there is a "central reflex" determining the control of the muscle groups, i.e.

muscle behaviour is patterned by the C.N.S. These patterns are inherent developments of inborn conditioned reflexes, predestined in foetal life. An inhibition of central control will thus upset the muscular balance. Gwynne Evans associates immobile palatolingual with immobile orofacial musculature, as in so-called "adenoid facies".

It can be put forward as a plausible explanation of snoring that during sleep there is a fall in adrenal secretion: this leads to a rise in parasympathetic over sympathetic action, and therefore a diminution of tone in the palatal structures.

In sleep there is said to be a rhythmic variation of depth: at first considerable depth, then lighter sleep and then before waking another increase in depth. If this is true one would expect snoring to occur more readily early in sleep and then just before waking. Actually severe sufferers snore all the time.

In anesthetized patients it has been said that a real snore does not occur—but this is not true—at any rate sounds just like snoring are heard. Dr. Vevers of the Zoological Society has told me that he has heard a chimpanzee snore under an anæsthetic.

Other factors influencing the position and tone of the glossopharyngeal structures.—Certain conditions other than that of nasal obstruction lead to slight œdema of the palatal mucosa, or loss of tone in the muscular velum. Slight pharyngitis from working indoors, and from smoking, obesity, plethoric tendencies, and allergic manifestations have all been listed as aggravating causes. One observer has described snoring as one of the diagnostic signs of leprosy of the pharynx; if this were so, one would expect any granulomatous condition in the pharynx to lead to snoring. That a mobile palate is essential for snoring is utilized by speech therapists in the "snorting test" in training cleft-palate patients.

I must mention that in America some prominence is given to the psychological aspect of causation. An article entitled "Does a contented person snore?" shows the trend of thought. It is considered that some snorers stop the habit when on holiday, and others have cycles of snoring periods regulated by psychological and endocrine factors. Personally I think this unlikely, but Gwynne Evans' theory of "central reflexes" makes it not impossible for basal or even higher centres to decide if and when we snore.

Ætiology.—At first thought it appears that the explanation of snoring would be simple enough. Any organic condition causing nasal obstruction would lead to mouth breathing, and a snore would be unavoidable. But this is not so: mouth breathers do not all snore. Causes must be divided into organic and functional or, better, dysfunctional, and although the main predisposing cause may be organic there is usually a dysfunctional cause as well.

A. Organic causes.—(1) *Nasal obstruction:* It is often the minor degrees of obstruction which lead to enough mouth breathing to initiate snoring, e.g. slight deflection of the septum, collapsed alæ nasi, or moderate mucosal congestion.

Dr. Vevers tells me that although he has never heard a wild wolf snore, many domestic dogs, all descended from the wolf, do so. He imagines this occurs in breeds with malformation in the nose and nasopharynx, caused by such conditions as achondroplasia, as seen in pekinese, &c.

(2) *Pathological changes in the pharynx* may make the soft palate and faucial pillars more liable to be in a suitable physical state for snoring to be initiated.

B. "Functional derangements"—or "*Dysfunctions*"—of the "central reflex" governing the tone of the glosso-pharyngeal musculature.

Age-groups.—There are three main eras of snoring: in the child, the adult and the elderly person. In children the majority are cured by removal of their adenoids and tonsils. The exceptions to cure include the persistent mouth breathers of "functional" origin and those with infective or allergic rhinosinusitis.

The adult who starts snoring usually does so from some organic cause. Women snorers appear to be as numerous as men.

The largest group of sufferers are elderly men and women. Lack of tone seems to be the fundamental cause.

TREATMENT

A. Irrational methods.—Chief amongst these is amputation of the uvula, which used to be a popular practice. Removal very rarely gives much relief, but it may modify the degree and pitch of the snore.

B. Rational methods.—(1) *Remove or prevent nasal obstruction*, and so allow for cessation of mouth breathing. In some instances simple decongestive nasal drops before retiring will allow a peaceful night. In others various nasal operations may have to be performed. Benadryl is useful for some persons.

(2) *Change position of head* to prevent tongue falling back. Many persons snore only when on their backs, and on some occasions the uncomfortable procedure of a cotton reel sewn into the back of the pyjamas is efficacious.

(3) *Alter position of tongue, soft palate and/or jaws*, by breathing, swallowing and phonetic exercises, or by orthodontic "splints". The former aim at training the central nervous system to regain proper neuromuscular control. The latter alter the shape of the mouth and thus try to guard against the tongue and fauces falling into the "critical" position.

In all these three groups it is necessary to regain proper central control of the soft palate, and break the habit of an inverted reflex.

(4) *Keep mouth closed during sleep*: This is done by wearing an "Andresen" splint (which is well tolerated by most children, but less so by an adult) or by the simple expedient of a strip of adhesive plaster across the corner of the mouth. After a short time this is well tolerated by many patients. An adequate nasal airway is of course essential.

C. *Altering texture of soft palate and faucial pillars*.—Injection of a sclerosing solution into the pillars is advocated by Jerome Strauss, though this enthusiastic surgeon has not been able to claim a high percentage of cures so far.

However, I feel we surgeons may have helped many potential future snorers by our effort at removal of their tonsils and adenoids—leaving them with nothing but a fixed fibrous band instead of nice mobile soft palate and faucial pillars!

CONCLUSIONS

Snoring is a symptom of unbalanced breathing, caused by a combination of several physical conditions, some brought about by pathological and other by physiological disorders. Remedies must aim at preventing all these causes and not only one.

[December 5, 1947]

Film Showing Organic Disorders of the Larynx.

G. H. Bateman said that some months ago he had shown the Section a film illustrating bronchial neoplasms which Dr. Paul H. Holinger, of St. Luke's Hospital in Chicago, had taken. Dr. Holinger had now sent him a film entitled "Organic Disorders of the Larynx", which had been prepared from Dr. Holinger's own cases and had been sub-edited and annotated for showing to medical students and speech therapists. He had had the opportunity recently of talking with Dr. Holinger about his method of taking films by indirect laryngoscopy. The patient sat upright facing the operator who used the same camera and apparatus as was used for the direct pictures. The laryngoscopic tube was used and a mirror obliquely disposed at the end of this tube. Thus the mouth did not appear in the films as the view is confined to the mirror and its reflections. In direct laryngoscopy the mirror was removed and the laryngoscope tube introduced in the ordinary way, with the patient having his back to the surgeon. All the pictures were taken under local anaesthesia.

The result of this change of position of the patient is that the right cord will be on the right of the screen in the direct pictures and on the left in the indirect pictures.

A considerable range of pathological conditions of the larynx is shown and the treatment mentioned though no details of treatment are given in the film. The colour is very accurate and the film is an admirable method of demonstrating the pathology of the larynx to students.

Bell Telephone Film of the Laryngeal Movements.

V. E. Negus showed a film taken by indirect laryngoscopy with an ultra-rapid camera. The pictures were taken at 4,000 frames per second and slowed down to normal rate so as to show the laryngeal movements in slow motion. Mr. Negus said that this film differed from the beautiful film they had just seen in that it showed the normal mechanism instead of diseased states.

Many of those present, like himself, had no doubt made use of the stroboscope, from which a great deal of help could be obtained in observing the laryngeal mechanism. On the evidence of the stroboscope was based a certain amount of the criticism he would make of the film. The stroboscope consisted of a perforated disc so rotated in front of a lamp that the light could be interrupted a certain number of times per second; the speed could be altered at will. If the speed were 200 times per second, for example, it was possible to illuminate the larynx at exactly the same rate as that of the sound produced. If the pitch were at the rate of 200 vibrations per second the vocal cords for 1/400th of a second would be moving towards the mid-line and for 1/400th of a second away from the mid-line. If only one phase were illuminated the cords appeared to be stationary. By varying the speed

the light of the stroboscope could be made to interrupt at 201 times per second, while the patient was still phonating at 200 double vibrations. Every time, therefore, the cords would be illuminated a little sooner or a little later than before, and it was possible to see, for instance, whether the arytenoids came firmly together or whether they remained separated; so that actually an even slower picture could be obtained than with this film.

The normal mechanism of phonation consisted of approximation and separation of the vocal folds. In this the arytenoid cartilages should come together and should remain firmly apposed and should not vibrate. There were theoretically two ways of raising the pitch: One was by *stretching and tightening the cords*; and the other by *increased contraction of the arytenoid muscles*, whereby the elasticity of the glottic margins increased and the vocal cords therefore recoiled more rapidly than when the muscles were less powerfully contracted. When this contraction took place the pull of the adductor and tensor muscles was so strong that the fold was shortened. The rise of pitch depended on the increase of elasticity of the thyro-arytenoid muscles, due to their increased contraction, and not on stretching of the cords.

A second point was the position of the arytenoid. How the arytenoid cartilage remained in a certain position would be shown in the film; also the eversion of the vocal folds, which did not merely separate in a lateral direction from each other but had a sort of rolling movement. Also, as the vocal cords shortened, the aryepiglottic folds would be observed coming forward. Looking from above, the epiglottis appeared to tilt forward and to display more of the vocal fold as the pitch rose.

A third part of this film showed how the glottis was blown open. If the thyro-arytenoids contracted and held the cords together the glottis would suddenly be blown open on phonation, and then the elasticity of the glottic margins was sufficient to bring the folds together again, the repetition of this process producing a sound of a fixed pitch. In some cases it was only a short part of the glottis that opened. In another part of this film would be seen the mechanism of whispering.

If by some means there was lack of apposition of the arytenoid cartilages, and if the vocal processes were kept slightly apart, there would be a disturbance in the vibration of the cords. If the posterior ends were not kept close together the vocal cords would bang together and impinge unduly at their centres. In the higher pitches it would be noticed that only the margin of the cords separated, without the eversion which was shown in the lower pitches. The last part of the first reel showed vibration at 850 vibrations per second.

One point of interest in the second reel was that one vocal cord was seen to be vibrating *more than the other*. It was possible for the patient to produce a sound almost entirely by vibration of one vocal cord, the other remaining stationary. It might be because of this that there were very few singers with completely pure tones. Another effect shown was the rise of pitch when the patient breathed helium. If helium with oxygen were given to a patient with dyspnoea it could be determined whether it were given efficiently by the manner in which the pitch of the voice rose.

V. E. Negus added that in the textbook "Diseases of the Nose and Throat", by the late Sir StClair Thomson, fig. 33 showed the imperfect view of the larynx obtained by the beginner because the epiglottis overhung part of the vocal cords and made the view incomplete. If one held a laryngeal mirror against the hard palate and got the patient to make the sound "E" it was often possible to see the whole of the vocal cord, including the anterior commissure, without causing the patient to feel sick. The mechanics of the elevation of the larynx were somewhat complicated. As the pitch rose the larynx was usually elevated to a certain extent and brought up towards the hyoid, and in doing so was tilted so that the vocal cords came to be more at right angles to the axis than at low pitches.

Mr. Forster had spoken of a phenomenon of the right arytenoid in phonation being well in front of the left. One might be led into error if one based a supposition of paralysis on the fact that one vocal cord did not move as well as the other; it might be simply a functional process. In all cases of functional disability the Wrisberg cartilage would be upstanding and in the usual position, but in all cases of organic paralysis, the posticus being the first to be affected, this cartilage would fall forward, and the aryepiglottic fold would obscure the vocal cord. It was quite easy to distinguish between the two conditions. On the one hand the patient might have a mediastinal mass, or else the whole laryngeal condition might be functional and due to a slight disorder of muscular effort; it was difficult for the contraction of the two sides of the larynx to be equally balanced.

The vocal cords themselves were of such small mass that they could not produce much sound. The sound was not made by vibrations similar to those of a string, but by the interruption of the air current into puffs. Only by the modification and amplification of resonators was speech and voiced sound produced.

Section of Otology

President—DONALD WATSON, F.R.C.S.

[November 7, 1947]

Progress in the Treatment of Mastoid Infection and some of its Complications

PRESIDENT'S ADDRESS

By DONALD WATSON, F.R.C.S.

THE discovery of antibiotics has simplified and, with the advent of others, will increasingly simplify the treatment of acute conditions of surgery.

In his Presidential Address two years ago Graham Brown (1945) said:

"I believe the opportunities for mastoid surgery are gradually decreasing in proportion as the prophylactic measures against the incidence and spread of aural disease increase. Indeed, the time may not be far distant when intracranial complications of otitic origin will be considered rare phenomena."

My introduction to mastoid surgery was in 1920 in Edinburgh, where I worked for two years under Mr. J. S. Fraser.

His method of treating the acute mastoid cavity, after a most thorough removal of all infected bone, was to cleanse it with hot hydrogen peroxide and to pack the wound with iodoform gauze, leaving an adequate drain at the lower end after closure of the rest of the wound. The pack was removed on the third day, the wound was repacked and continued to discharge more or less for three to four weeks before healing took place. This ideal was not always attained: often the wound broke down, when eusol syringing was carried out twice daily. An infected, broken-down wound meant prolonged treatment, sometimes of many months' duration.

Going to Bradford in 1922, for four or five years I tried other methods then practised, such as the blood clot method—closure without drainage. This was very unsatisfactory, as the wound usually broke down. Then there was the method of leaving the wound almost entirely open, packing it, and allowing it to heal by granulation tissue from the bottom. This was a tedious method, but it certainly obliterated the cavity, and there were no recurrences. The subsequent depression over the mastoid is unsightly. Nevertheless, it is a method practised even to-day in certain clinics.

Next came the use of various antiseptics with packing. Of these T.C.P., first produced about 1922, was the most successful in my hands.

It was in 1928 that I discarded bipp and reverted to the Carrel-Dakin method of flushing the wound with eusol and drainage by rubber tubes. This method was employed almost exclusively until early in 1933. It was a safe method—took time to do the dressings, but obliterated the cavity. T.C.P. was used as a final lotion for dressing the wound.

In the February of 1933 a severe influenza epidemic occurred and, at its height, no less than 53 cases of acute mastoiditis were in hospital at the same time. Most of these were severely infected, some had complications, and the labour of dressing them was a tremendous strain on our nursing resources.

I decided to go back to using bipp in the liquid form, with a small gauze drain at the lower end of the wound. The bipp in the paste form used a few years previously was too solid and I am sure it caused the recurrences. The liquid bipp plus drainage for two or three days greatly lessened the number of recurrences.

This bipp method, published by Mr. Herbert Tilley (1919), Holt Diggle and Gilhespy (1921), supported by Macnab of Johannesburg and others, was the most successful in my hands and also in the hands of other surgeons, and I have used it until 1944. The great majority of cases were discharged, with the wound healed, in a fortnight. Packing the wound was dispensed with.

Secondary suture.—When there was osteomyelitis of the squamous temporal and of the occipital bone, it might be necessary to enlarge the mastoid wound by one or more radial incisions, backwards or upwards and backwards.

In such wounds and also in widespread and severely infected cases, a bipp pack left undisturbed for five or six days enabled one to do the secondary suture, which was so important. The wound must be closed in five to six days, otherwise, owing to shrinkage and curling of the flaps, it may be impossible.

Even with bipp sometimes a child's wound would not heal. Occasionally I gave these tardy cases a weekly dose of tuberculin in a glass of milk, an hour or so before breakfast. This has a most beneficial effect on these slowly healing wounds.

To-day the universal practice is to dust the mastoid wound lightly with penicillin and sulphathiazole powder and close it, except perhaps for a small gauze drain at the lower end left in situ for a couple of days. Most cases are discharged healed by the twelfth day with a dry ear. In severe infections, the giving of sulphonamides and penicillin is an added safeguard. This modern treatment has shortened the stay in hospital tremendously. Whether the aditus remains open and recurrences are to be expected more frequently, I am doubtful, but the great saving of time and worry outweighs this possibility. Even secondary suture in mastoid surgery will, I believe, also become a relic of the past.

Lateral sinus thrombosis.—In these days of antibiotics and chemotherapy cases without cerebral complications should all survive.

With regard to ligation of the jugular vein: years ago, Mr. Ballance said there were occasions demanding ligation, and there were occasions where the local condition in the sinus could be dealt with efficiently without ligation. A more rational opinion one could not have on this problem. I was always prepared to ligate the vein if occasion arose, as I am firmly convinced of the efficacy of this procedure. Even with the aid of chemotherapy I should not hesitate to ligate the vein if the case had symptoms of pyæmia with infarction of the lung. Otherwise treatment of the local condition of the sinus is all that is necessary.

To obtain the best results in lateral sinus cases, surgeons have had to do the dressings themselves for many days, but we got good results, even as high as 80% recoveries in cases without cerebral complications.

The accompanying septicæmia is the danger in sinus thrombosis. Antitoxic sera of all kinds have been tried. The best, I believe, was the scarlatinal antitoxin. Quinine was also used. It did one good thing. Frequently a fixation abscess occurred at the site of the injection. One was always pleased to see this. These cases entail long and tedious treatment and careful observation.

I have opened 11 abscesses including an infected knee-joint and an ankle-joint in one boy, and he recovered with no disability except a stiff knee.

Lateral sinus thrombosis cases have given us many interesting struggles. Pus in the internal jugular vein was not a rare occurrence.

With the continuation of rigors or swinging temperature—a common occurrence—one has frequently traced the lateral sinus back to the torcular Herophili before effecting a cure, this process requiring three or more operations. Mr. J. S. Fraser always packed the interior of the open sinus with iodoform wool, but I understand some surgeons did not believe in this rational procedure.

I have had only one case of cavernous sinus thrombosis as a complication—a man aged 28. I am informed that after his recovery he lived for a further six months and died at home with symptoms of brain abscess.

Perhaps my most interesting case was one in which an abscess developed at the root of the neck, just between the clavicles. I waited before opening and packing this one. On removing the dressing two days later I was alarmed when I looked inside, as there was no reaction in the walls of the cavity and everything seemed to be pulsating. I repacked that cavity with bipp and left it. This child of 5 had an interesting reflex. Her lateral sinus had been opened almost to the torcular, and each day as I dressed her and touched the sinus wall she complained of pain on her nose—a reflex through the meningeal branches of the fifth nerve. She eventually recovered after having been on sulphathiazole continually for six weeks and having taken nearly 800 grammes.

The actual percentage of cure, in cases where lateral sinus thrombosis arises, is high, but in the future it may be expected, with the early use of chemotherapy, that this complication will be progressively more rare. Apart from the Schwartze or other original operation there should be next to no need of any added major operative procedure and, consequently, a greatly lessened stay in hospital.

Meningitis is a fairly common complication of mastoiditis. Its early diagnosis is important.

Progress in the treatment of meningitis is so intimately dependent upon early diagnosis that I shall now discuss the sign upon which early diagnosis depends. The picture of meningitis I need not detail.

The most important sign in my opinion is early stiffness of the neck. You know how easily anyone, and especially a young child, is able to flex the neck, put the chin on the chest, and then move the chin laterally—i.e. rotation. The slightest restriction of extreme flexion and rotation is demonstrable by comparison with a normal patient, and is the most valuable sign.

In a paper on meningitis, T. B. Layton (1935) laid great stress on this early stiffness of the neck. In spite of views to the contrary, I think this sign is always present if it is looked for in the manner which he described.

On one occasion I was called to a fever hospital to see a nurse. Three days previously she had a pimple just inside her nose, and as she was going to a dance that evening she pricked it. When I saw her, she was lying on her back, her head propped up by pillows, with violent headache and a high temperature. I took the pillows away and tested her neck. She could bend her neck easily up to the angle of rest on the pillows, but beyond that it was rigid. Diagnosis—meningitis. The doctor in charge said “nonsense, she can flex her head easily,” and so she could up to the angle of rest. We did a lumbar puncture: the C.S.F. was very cloudy—she died in 24 hours. I mention this as one of the pitfalls in testing the neck for stiffness.

Twenty-five years ago, meningitis was a deadly complication. About 80% or more of the cases died, and although one's luck varied, the results were poor, or at any rate mixed, until the sulphonamides arrived. In 1929 I had three cases in succession who survived but this was just a flash in the pan.

My personal results improved after using the technique of T. B. Layton (1935), that is early operation to remove the focus of infection, with free removal of the

tegmen, keeping the wound open by means of stitching the flaps back, and flushing regularly with saline. As a modification, later I used hypertonic saline packs. Lumbar punctures were done daily, and sometimes twice daily. My figures improved to over 30% recovery with these methods. I also tried injecting the theca with various antiseptics, solganol and others, but it did not appear to affect the recovery rate.

In the early thirties, Neuman evolved an operation with a very wide removal of the tegmen tympani as far forward as the eustachian tube, elevation of the dura and exposure of the upper surface of the petrous, then wide removal of the tegmen antri. Ruttin (1934) using this method claims a 50% recovery. These were the best results published up to 1934. Sulphonamides increased the recovery rate greatly, up to 50%, and penicillin has improved it still further, until to-day the recovery rate is over 80% in uncomplicated cases.

TABLE I.—BENIGN FORMS OF OTOGENIC MENINGITIS (MYGIND, 1922)

Based upon the observation of 210 patients with meningitis of all forms, caused directly or indirectly by acute or chronic middle ear suppuration, over the past seventeen years.

Meningitis (uncomplicated)	Total	Recoveries	Percentage
„ plus sinusphlebitis	115	38	33.0
„ plus brain abscess*	42	16	38.1
„ plus subdural abscess	21	4	19.0
„ plus subdural abscess plus brain abscess	2	0	0.0
„ plus sinusphlebitis plus brain abscess	15	0	0.0
„ plus sinusphlebitis plus subdural abscess	6	0	0.0
„ plus sinusphlebitis plus brain abscess*	7	1	14.3
	210	59	

*Including encephalitis.

= 28% recovery.

These are the best, and by far the most complete results published in the *J.L.O.* up to 1922. 28% over-all recovery.

My personal results for seven years after 1922 show a 19.6% recovery. This is just less than 20% against Mygind's 28% all cases.

TABLE II.—TWENTY-ONE CASES OF OTOGENIC MENINGITIS SHOWING THE TIME-RELATION OF OPERATION ON THE EAR TO THE COURSE OF THE ILLNESS, THE PREVIOUS HISTORY, THE RESULT AND THE CAUSE OF DEATH (CAIRNS, 1946).

Operation	No. of cases	Previous otitis	Recovered	Died	Cause of death
Mastoidectomy before meningitis	3	2	2	1	Abscess
Mastoidectomy at height of meningitis	3	1 (? 2)	2	1	Heart failure and inhalation pneumonia
Myringotomy at height of meningitis	1	1	1	0	
Mastoidectomy during convalescence	2	1	2	0	
No operation	13	4	9	4	
	22		16	6	

= 72.72% recovery.

One patient (Case II) had two operations.

Previous otitis = a previous history of infection of the ear.

This paper was the result of experimental research by Professor Cairns and his team. As an experiment it is a remarkable tribute to the power of present-day chemotherapy. I should like to draw attention to one or two facts in this table, but not in a critical vein.

It is interesting to note that in those cases: (a) Operated on (9 in all) only 2 died—77.7% recovery; (b) not operated on (13 in all) 4 died—69% recovery.

This is in spite of the fact that in 6 of (a) no pre-operative chemotherapy had been carried out.

Professor Cairns states that in the 13 cases operation could not have altered the course of the disease. This statement is debatable. He postulates two questions: (a) Is the brain abscess produced concomitantly with the meningitis? (b) Is it produced later?

Nobody can answer these questions definitely, but, if it is later, and we know it often is by direct extension from the mastoid through the tegmen, then early mastoidectomy might have saved the two brain abscess cases, and even the acute cerebral oedema.

I have no knowledge, but I can quite appreciate the diffidence of aural surgeons advising operative interference during this experiment—evidently they were not consulted in some of the cases.

In this experiment it will be observed that brain abscess, even in the hands of a neurosurgeon, caused most of the deaths—3 out of 6.

TABLE III.—A SERIES OF 13 CASES OF MASTOIDITIS WITH MENINGITIS FROM 1.1.44 TO 1.9.47. 2 DEATHS IN 13—84.6% RECOVERY. DONALD WATSON, BRADFORD

Date	Name	C.S. fluid	Organism	Treatment	Findings
13.1.44	J. C. B.	Cells + (5)	Streptococcal	Sulph.	Mastoiditis and meningitis
10.4.44	H. B.	Cells + (6)	Small coagulum	Sulph.	Mastoiditis and brain abscess
19.5.44	L. J.	(1)	No growth	Sulph.	Mastoiditis and meningitis
9.1.45	G. O.	Cells ++ (2)	No growth	Sulph.	Mastoiditis and meningitis
18.4.45	A. P.	Cells + (3)	Pneumococci	Sulph. and pen. intrathecal	Mastoiditis and meningitis
18.9.45	V. N.	Cells ++ (5)	No growth	Sulph. and pen. intrathecal	Mastoiditis and meningitis
29.12.45	M. B.	Turbid (3)	Streptococcal	Sulph. and pen.	Mastoiditis and meningitis
7.1.46	R. P.	Turbid cells + (3)	Streptococcal	Sulph. and pen. intrathecal	Meningitis
6.2.46	J. B.	Cells + (3)	No growth	Sulph. and pen.	Mastoiditis and meningitis; lateral sinus thrombosis ligature of vein
12.2.46	G. B.	Cells ++ (1)	No growth	Sulph. and pen.	Mastoiditis and meningitis (died 14th)
4.9.46	W. S.	Turbid (2)	No growth	Pen.	Mastoiditis and meningitis (died 11th), oedema of lungs, duodenal case
23.12.46	R. C.	Cells + (8)	No growth	Pen.	Mastoiditis and meningitis
19.8.47	M. F.	Clear (2)	No growth	Sulph. and pen.	Mastoiditis and meningitis

The figures in brackets indicate the number of lumbar punctures performed. Sulphathiazole was used in every case.

This table emphasizes the value of chemotherapy, which was given in all cases before operation for about twelve hours, and continued after operation until the T. had remained normal for two days. The recovery rate of 84.6% compared with my earlier records up to 1927 of 20% recovery rate needs no comment. All the cases except one (7.1.46. R. P.) had mass mastoidectomy performed.

Labyrinthitis.—The subdivisions of this disease usually given in a textbook are somewhat bewildering.

The circumscribed type with the fistula sign is definite, as is the diffuse purulent type, but the serous types are not so definite and clinically do not matter—if left alone they recover. Lastly, there is the latent diffuse type—probably with a dead labyrinth.

As a complication of acute mastoiditis, I have seen only one case of diffuse purulent labyrinthitis with its severe symptoms, a small boy of 6. He had an extremely severe mastoid infection with labyrinthitis, lateral sinus thrombosis and meningitis. He died twenty-four hours after admission. I had performed a Schwartze operation in the meantime, but his was a fulminating generalized infection. At the post-mortem the saccus endolymphaticus was a bag of pus—the only case I have seen. I am aware that, through the years, recoveries of a few cases of acute diffuse labyrinthitis have been reported in the journals. This rare complication of mastoiditis—primary acute diffuse purulent labyrinthitis—is almost certainly a blood-borne infection as is primary pan-opthalmitis.

I shall return to serous labyrinthitis in acute mastoiditis. In the following remarks, I shall discuss two problems:

(1) The inadvisability of testing the labyrinth by caloric and rotation tests in cases of mastoiditis with labyrinthine symptoms, either acute or chronic.

(2) The relationship of labyrinthitis and meningitis. This problem appears to me to be more readily studied and understood in acute than in chronic mastoiditis.

The accepted views on labyrinthitis were clearly expressed by E. D. D. Davis (1928). He stated:

"The records of cases of meningitis which followed chronic suppuration reported by Logan-Turner, Fraser, Jenkins and myself have shown that the symptoms and signs of labyrinthitis were present in a very large proportion. Vertigo, tinnitus, nystagmus and a marked degree of deafness accompanied by headache and fever with an increase of cells in the cerebrospinal fluid call for a translabyrinthine drainage of the meninges without hesitation. There are certain signs of the spread of infection which forecast coming events. *Labyrinthitis is such a sign, and it requires careful investigation and prompt action as soon as it becomes apparent.*"

Tweedie (1934), who knew as much as anyone of his generation about the physiology of the labyrinth, supports the above view. In a paper published in 1934 he stated that in inflammatory lesions of the labyrinth—as in inflammation of any other organ—the normal responses to stimuli were upset, and all sorts of contradictory results obtained. In his 7-point summary of the tests, in point 6 he stated "that an attempt should still be made to assess the inference of spontaneous nystagmus in cases of acute otitis media". Previously he states that it is in these acute cases where we require assistance in assessing the amount of labyrinthitis that we shrink from applying the tests, and that generally we restrict the use of the labyrinth tests to chronic inflammatory cases of otitis media to determine whether or not the labyrinth is still functional.

I am of opinion that the above views are entirely wrong, and if carried into practice increase the danger to life in the treatment of labyrinthitis whether associated with acute or chronic mastoiditis. During the four years 1922–25 I carried out the usual cold caloric and rotation tests (Cold water (65° F., 17° C.) and the Bárány chair) in all cases of chronic mastoiditis. I operated on 3 cases with signs of labyrinthitis, and all 3 cases died of meningitis. During these years my colleague had no deaths. On careful investigation I found that the difference between his technique and mine was that he did not test any cases of labyrinthitis, whereas I did both caloric and rotation tests. I think it was the late Mr. Albert Gray who said that the labyrinthine capsule had great powers of defence and was capable of looking after itself in the presence of aural infection. As a result of these practical and theoretical considerations, I decided to stop testing the labyrinthine function, and wherever symptoms suggestive of labyrinthine upset occurred, to put the patient at rest, sand-bagging the head. During the twenty-one years that have passed since then, though I have had a number of cases of circumscribed labyrinthitis with the fistula sign, I have had no deaths from labyrinthitis in chronic mastoid disease.

It is my emphatic opinion that cases of mastoid disease in which labyrinthitis is suspected should be left at rest and that this complication will disappear in about three weeks. Several reasons may be put forward for regarding the widespread practice of testing the functions of the labyrinth in those cases as both useless and dangerous.

The labyrinth is endowed by Nature with strong defensive powers against infection. It is separated from the middle ear by a thin layer of bone—the stapes in the oval window, and the round window—and has to resist infection from a vast number of cases of middle-ear suppuration and mastoiditis annually. I have diagnosed about 6 cases of petrositis, but none complicated by labyrinthitis; cases of Gradenigo's syndrome without labyrinthitis; cases of herpes of the geniculate ganglion; all of which had vestibular upset, but all recovered. In chronic mastoiditis, I have had a number of cases of circumscribed labyrinthitis with the fistula sign. Since 1926 not

one has developed diffuse labyrinthitis. Surely all these points are evidence of its great resistance to infection.

The rarity of severe labyrinthine infection compared to the vast number of middle-ear infections bears witness to the efficiency of its defensive mechanism. Where it becomes mildly infected and Nature has succeeded in walling off the infection it is surely dangerous to subject the patient to a series of tests which, I believe, are well calculated to break down the natural barriers and produce diffuse labyrinthitis, just as perforation of an acutely inflamed appendix sets up dangerous peritonitis. Tests of functional activity suitable in physiological conditions may be fraught with danger in pathological conditions and should be avoided. If active surgical treatment is indicated for the mastoiditis it should be carried out, but the labyrinthine upset should be left undisturbed and allowed to settle.

There is an analogy between the eye and the ear. Both are developed from the ectoderm. Primary acute pan-ophthalmitis is rare. The lesser degrees of inflammation interfering with function are more common, similar to cases of serous labyrinthitis which, if left alone, and rested will recover.

To conclude this portion of my paper, I believe that the use of these physiological tests on the labyrinth is the direct cause of the many cases of diffuse purulent labyrinthitis in chronic aural suppuration and the reason of the many translabyrinthine operations. These operations, with their fatalities, are a blot on our escutcheon.

I wish now to return to serous labyrinthitis in acute mastoiditis and to discuss the second problem, i.e. the relationship between labyrinthitis and meningitis.

Apart from the single case of acute purulent labyrinthitis already mentioned, I have seen a number of cases of acute mastoiditis with labyrinthine symptoms. One of these cases, about 1933, caused me much worry, and also gave me the key to this problem. She had an acute mastoiditis with very marked signs of labyrinthitis plus meningitis and a temperature of 104° F. Her symptoms subsided after the Schwartze operation had been performed. This wound was left open and treated according to Layton's technique. Lumbar puncture showed increased pressure in the C.S.F. with some increase of cells but no organisms. This patient not merely recovered but she regained her hearing. She could not have had a purulent labyrinthitis: it had been of a serous type, yet her labyrinthine symptoms had been so extreme that I diagnosed her as a fulminating case of acute diffuse purulent labyrinthitis plus meningitis, and gave her father, who was a doctor, a fatal prognosis.

In this case there were marked symptoms of labyrinthitis plus meningitis. These should be regarded as two manifestations or complications of the parent acute otitis media—twins if you like, but not Siamese twins—separate entities.

In many clinics of the Continent and elsewhere, *if such a case of labyrinthitis plus meningitis with an increased cell count had occurred, labyrinthine drainage would have been done at once*, on the supposition that the meningitis develops from the labyrinthitis and this, I think, is wrong. Nearly all are simply cases of serous labyrinthine upset—the meningitis is the danger. It must be treated and has nothing whatsoever to do with the labyrinthine condition. The labyrinthitis heretofore has been regarded as the danger causing the meningitis.

There is one other condition that *does* occur, that is induced purulent diffuse labyrinthitis induced by operative procedure or injury, and this applies equally to the eye. Labyrinthitis induced by operation may occur once in every surgeon's life, but it should be only once, and to-day, with chemotherapy, the patient should live. When induced purulent diffuse labyrinthitis is produced, it infects the meninges. This sequence has frequently occurred, and is responsible for most of the work and written papers on labyrinthitis in the past. There has been no progress in any published material on labyrinthitis.

SUMMARY

(1) *Infection*.—The labyrinth is very resistant to infection, and diffuse purulent labyrinthitis is rare and is, or should be, almost entirely a primary disease.

(2) *Tests*.—(a) Diffuse purulent labyrinthitis, following labyrinthine tests, I regard as induced.

(b) The practice of testing the labyrinth is due to a confusion of thought. Physiological tests of function have been used on the labyrinth when it is in a pathological state. They are not clinical tests, and should be discontinued.

(3) *Relationship of labyrinthitis to meningitis*.—(a) Even when labyrinthine symptoms are very severe, they may not be due to a purulent infection of the labyrinth. They are simply a labyrinthine upset—"serous labyrinthitis" if you like the term.

(b) This labyrinthine disorder will recover without any interference with the labyrinth, provided, of course, the patient recovers from the original mastoiditis and its other complications.

(c) Meningitis is not as a rule caused by labyrinthitis as many observers think. It is always a primary complication of mastoiditis.

(d) Labyrinthine upset may be associated with meningitis, but the two conditions are entirely distinct. This is the fundamental point in the understanding of this problem.

The complication of brain abscess has not been included. It is a difficult problem. There has been marked progress in its prevention since its parent, the acute mastoid, is becoming more scarce because of chemotherapy.

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Mr. E. D. D. Davis said that it was most important to decide when to operate on a case of acute mastoiditis. The operation should be delayed if possible until the mastoiditis was localized and suppuration was present. If the mastoid were opened too soon, healing was prolonged, and the inflammatory condition appeared to spread. On the other hand an abscess healed rapidly. If all the air cells were opened in the simple complete mastoid operation a drainage tube for forty-eight hours only was all that was necessary. It was the unopened suppurating air cell which caused trouble and not the lack of drainage. Packing the wound with gauze led to a surface slough and secondary sepsis and must be avoided, a drainage tube was far better.

When meningitis was threatened the wound was left open but not packed. Rigidity or slight stiffness of the neck was a too late sign. Very few cases of meningitis with rigidity of the neck recovered. The rigidity was caused by a collection of purulent fluid in the basal cisterna and around the crura cerebri. The examination of the cerebrospinal fluid was the only way to make an early diagnosis. Cases of meningitis arising from a blood-borne infection died very rapidly as in the case the President had mentioned.

In 1922 it was agreed that an operation on the labyrinth for labyrinthitis should not be done before the labyrinthitis was localized. A threatened or established meningitis demanded operation.

Lund of Copenhagen and others relied on the examination of the cerebrospinal fluid. If the count increased it was an indication for operation. A large number of labyrinth operations had been done because of the fear of meningitis.

Children and young adults were more susceptible to meningitis than old people. The unexplained severe headache with a rise of temperature and pulse, the cellular mastoid pouring serous fluid with deep-seated pus in the cells behind the facial nerve, the mastoid following scarlet fever and measles

all pointed to the possibility of meningitis. Treatment by sulphonamides and penicillin had improved the prognosis of meningitis.

Mr. T. M. Boyle made a plea for the use of heparin in a small number of cases of lateral sinus thrombosis. He cited the case of a girl aged 15 who had the lateral sinus drained and continued to have rigors for about a week afterwards. She was having large doses of penicillin and sulphonamides. Then a general surgeon put her on heparin, and from that day she made a rapid recovery. He would not say that all cases should have heparin, but those cases not responding to treatment. In another small group of cases of mastoiditis there were resistant organisms, *B. pyocyaneus* being one of the offenders, and here he thought phenoxetol, a proprietary preparation, was of great value. He recalled a case which had had the mastoid opened about ten years ago, and later developed a recurrence: an attack of mastoiditis with a green discharge. It dried up but recurred on several occasions. The mastoid was opened and the drainage tube inserted and phenoxetol applied in the cavity. Within three days the discharge from the external meatus was sterile, and within six days the middle ear was dry.

Mr. W. H. Bradbeer said, with regard to latent labyrinthitis, that two patients in whom he suspected that the labyrinth was dead both developed meningitis following operation. One was a mild case and recovered. In the other a very severe meningitis developed, and eventually a cerebellar abscess, but this case also recovered after opening the labyrinth and draining the abscess. If one was doing a radical mastoid operation with a dead labyrinth he had come to the conclusion that one should open the labyrinth as well, but after what the President had told them he was uncertain on that point. He thought they would still see chronic ears, and one came across children in school clinics with chronic otorrhœa and with an attic perforation.

Mr. F. McGuckin said he believed a cerebral abscess might arise at any stage of an otitis because of the possibility that a localized infection in a perivascular space might act as a preformed path. On the question of labyrinthitis he agreed almost unreservedly with the President's plea, in so far as the complication was related to acute otitis.

Mr. F. W. Watkyn-Thomas said that a danger in using heparin was that the clotting time was altered for a considerable time afterwards, which might give trouble should further surgery be needed. The justification for the use of heparin in sinus thrombosis would be to make sure that the antibiotics came into contact with the organism; an organism in the clot was safe from anything in the way of penicillin or sulphonamide treatment.

On the question of translabyrinthine drainage, since the use of sulphonamides he had only seen two cases of meningitis which were undoubtedly due to labyrinthine infection—at any rate they had certainly followed upon a labyrinthitis. In these two cases he refrained from translabyrinthine drainage because he felt that, if the cerebro-spinal fluid was released, it would be more difficult to keep up the requisite sulphonamide concentration. Both patients recovered. The translabyrinthine operation had been the greatest advance in treatment in its day, but now it would rarely, if ever, be necessary.

Mr. Ogilvy Reid referred to the rarity of such a complication as facial paralysis in acute mastoiditis or acute otitis media. He had in mind one or two recent cases which illustrated the difficulties which chemotherapy had introduced in the treatment of mastoid conditions and the way in which the picture was obscured. One case had had massive doses of penicillin and was apparently doing very well when a facial paralysis developed. He operated on the case and though he found no lesion relating to the facial nerve yet the facial paralysis began to recover after the operation.

Mr. R. R. Simpson asked what would be the President's attitude in the case of the labyrinth in the presence of otitis media with fistula signs? He himself did a radical mastoidectomy in such a case without interfering with the labyrinth at all, and so far he had never regretted it.

Mr. J. H. Otty felt sure that an adequate dosage was the essential in the use of the sulphonamides or penicillin, but it was equally important to tighten up the criteria of cure. These patients should not be let out of hospital unless the surgeon was satisfied, not only that the ear was dry but that the tympanic membrane had returned to normal and the hearing had been restored.

Mr. L. Graham Brown said that as a senior he felt that he had had a considerable experience of these cases during the past quarter of a century. The young practitioner only saw the question from his own recent experience, and naturally was a little perturbed as to what the treatment really ought to be. The time had now come when chemotherapy had taken a large part in the treatment of these affections. He wished to say with regard to chemotherapy that he used it only as an adjunct to

surgery. They were all aware that its application in the early stages of acute inflammation of the middle ear might be successful in relieving the condition, but also they knew the dangerous effects which might be brought about if it was used at a time when pus was formed in the middle ear or the mastoid bone or in the further complications of the disease. They were aware of the fatalities which occurred. Perhaps the mastoid operation would be followed by almost complete resolution, and then, some weeks afterwards, a brain abscess or meningitis occurred and the patient often died.

He had not operated on a case of labyrinthitis for many years—perhaps fifteen years. Cases in which there were signs of labyrinthine irritation in chronic disease of the mastoid, which flared up, he had dealt with by performing a radical mastoid at the opportune time, providing there was no evidence of the disease spreading to the meninges. Such cases had invariably got well. In view of the statements that these cases were rapidly diminishing, it was strange that Mr. Simson Hall should have seen recently several cases of lateral sinus thrombosis. He himself had not seen one for two or three years, but, curiously enough, he had three cases of meningitis, and these were cases of chronic mastoiditis, all of which, after removal of the focus in the mastoid—going no further, and putting them on chemotherapy—had recovered. The most important thing was to learn how and when to use chemotherapy.

Mr. Terence Cawthorne said that the high light of the President's Address was that he had had the courage years ago not to treat the labyrinth surgically in the early stages of an infection. Most of them had come to realize, now that they had recourse to chemotherapy and biotherapy, that early surgical treatment was wrong. He agreed with Mr. Layton who had suggested that chemotherapy should precede surgery even in chronic conditions where there was an acute flare-up.

Mr. H. S. Sharp said that in acute middle-ear disease he never gave chemotherapy unless he had first obtained drainage from the ear. Such cases were followed up very carefully by means of X-rays, and in adults, in addition to X-rays, by tests for deafness.

The President (Mr. Watson), in a brief reply, said that if there was any surgery to be done it must be done and done early, but on cases that had been on penicillin or sulphathiazole for three or four weeks there was no harm in operating if there was any doubt. Mr. Boyle had spoken of cases in which sulphathiazole and penicillin were given at the same time. That was an interesting point and one for discussion in the Section. He had seen two cases of meningitis in patients who had had too large doses of penicillin and sulphathiazole. The temperatures did not drop and he could not understand it. In one of the cases he stopped penicillin and the temperature dropped immediately, nothing else happened. In the other case he stopped sulphathiazole, with the same result. Some of these patients were "killed by kindness". Too much in the way of antibiotics could be given. Whether heparin counteracted the effects he could not say.

There had been a great deal of confusion about the chronic mastoid. People talked about labyrinthitis after they had been, he was sure, testing the cases. He himself would not have anything to do with testing, and if anyone talked about labyrinthitis after having done caloric, rotation or electrical testing he thought it a sequel. The plea he would put forward was to stop physiological tests. He drew an analogy from the heart. There was a tolerance test for the heart by which one observed the heart's function. This was carried out on a normal or near-normal heart. Would a clinician test a heart with valvular disease by means of these tolerance tests? Would he test a patient with a temperature of 102° F. whom he thought was developing endocarditis by asking him to run upstairs and down again? Of course he would not, but it was something like this that they had been doing in otology.

Section of Epidemiology and State Medicine

President—W. S. C. COPEMAN, O.B.E., F.R.C.P.

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The History of Cholera in Great Britain

By E. ASHWORTH UNDERWOOD, M.A., B.Sc., M.D., D.P.H., F.I.S.

ALTHOUGH Asiatic cholera did not visit the shores of this island until 1831, it had quite a respectable history long before that date. Macnamara [1]—an authority on the history of cholera in the East—thought that the disease may have existed in India in 400 B.C., and there are records of outbreaks in the fifteenth century. The devastating epidemic which prevailed in Lower Bengal in 1817 was the occasion of a number of short treatises on the subject by Europeans. Several of these were in the form of Latin theses presented to the Universities of Glasgow and Edinburgh [2]. Cholera reached Europe in 1829, and during 1830 and 1831 it was widespread in the countries of Central Europe. In Great Britain generally much interest was caused, and many fears aroused, by the continued existence in Europe of a disease which had until then been regarded as purely Asiatic. Preventive measures included the formation of a Central Board of Health with Sir Henry Hallford as President, and also of many local Boards of Health in different parts of the country.

About this time nearly all observers were much concerned about the indigenous "cholera" of Britain. It was known as "cholera nostras" and by various other names, and in certain features it did resemble Asiatic cholera. How were medical men to decide whether the true cholera had arrived, or whether they were still dealing with severe cases of cholera nostras? In order to settle this point the Central Board arranged for consultations to be given by medical men who had had experience of Asiatic cholera in the East. But the Eastern disease had a way of its own of settling the question, and when it did arrive the issue was never long in doubt.

The epidemic of 1831–32.—The first death from true Asiatic cholera in this country occurred in Sunderland on October 20, 1831. After a slight lull the disease took a heavy toll during the next few months, so that by January 9, 1832, 215 deaths from cholera alone had occurred in Sunderland. Cholera next appeared at Newcastle on December 7, 1831, and there it ran most of its course during the next few months. It did not finally exhaust itself until the summer, by which time there had been over 1,330 cases and 801 deaths. Gateshead and other Tyneside towns were attacked about Christmas or the New Year. Almost contemporaneously cholera appeared in Haddington. The first case occurred on December 17, and the next on the 25th. By February 23 there had been 125 cases with 54 deaths [3]. A little later the Tranent area was affected. The town of Tranent itself, with a population of 1,631 persons, had 204 cases and 64 deaths; and the villages of Cockenzie and Port Seton, and the town of Prestonpans, with a total population of 2,717 persons, had 195 cases and 36 deaths [4]. The small town of Musselburgh suffered a devastating attack, and between January 18 and February 22 there were over 400 cases and 202 deaths. The next areas to suffer the dire effects of the new disease were the large cities and the industrial centres—Edinburgh at the end of January, and Glasgow during the second week of February. In each the disease seemed to be exhausting itself about the beginning of the summer, but in July and August it sprang to life again in an even more violent form. In Glasgow alone there were 3,166 deaths—the highest mortality figures in the country, apart from London.

The epidemic in England fell much later than in Scotland, and really occurred in the summer and autumn. London was an exception, since the disease started there about February 14, and dragged on until the end of the year. The first important provincial city to be attacked was Hull. This was during the first week of April. The disease had broken out at Liverpool by the end of that month, and between then and the middle of July severe outbreaks had commenced in Manchester, Salford, Leeds, Plymouth, Sheffield, Nottingham, Bristol and Exeter. In a previous communication [5] I gave a full account, with a statistical discussion, of the epidemic as it affected the centres of population in Yorkshire. Hull and Goole were considered by the Central Board of Health as infected from April 6, but the first authentic cholera death in this area probably occurred on April 13. Alderson [6] described this outbreak well, and from his account it would appear that the disease did not really make itself felt until June, by which time it was epidemic throughout Yorkshire. Most deaths occurred at Leeds (702), Sheffield (402), Hull (300), and York (185). The writings dealing with the Sheffield outbreak were collected in 1921 by Stokes [7]. In Lancashire the

greatest number of deaths occurred in Liverpool (1,523), Manchester (706), Salford (216), and Warrington (168): The Manchester outbreak was well described by Gaultier [8].

From the numerous writings which appeared during these early months of 1832 it is evident that cholera was regarded as a visitation of Divine Providence on the vicious and an unfortunate catastrophe in the lives of the poor [9]. Most of the early reports emphasize the fact that the disease attacked those who were addicted to spirits, and that it was confined to the shacks and hovels of the new industrial districts. Doctors and nurses generally escaped infection, and the better-class districts were not affected.

Later in the year opinions began to change on these points. At any rate, nearly all the reports emphasize the frequency of unpaved streets and yards in the cholera areas; the absence of satisfactory arrangements for the removal of filth and the cleansing of privies and cesspools; and the necessity for lime-washing houses and adding nutritious articles to the diet [10]. There were some who denied the earlier opinions regarding the type of persons who were most readily infected. For example, Lawrie [11], in his essay on the cholera in Sunderland, Newcastle and Gateshead, says that it is not true that the poor and the dissipated are its only victims. He denies also that fear can predispose to the disease. "I do not believe", he says, "that fear ever gave a man Cholera or ever will. To the production of Cholera a regular chain of causes and effects is as necessary as to poisoning by prussic acid. The inhabitants of Gateshead fell asleep on the 25th December, in perfect security and devoid of panic, but before the sun rose on the 26th, fifty-five individuals had been seized, thirty-two of whom were destined not to see it set. For several days subsequent to the 27th, the panic of the inhabitants was greater than I have ever witnessed under any pestilence, while the new cases *decreased*, and on the 30th were as low as twenty". This passage is reminiscent of Boccaccio's celebrated description of the plague in Florence.

Of all the outbreaks during this momentous year, three stand out because of the havoc which they produced, or because of the fact that they have been well described. The Exeter outbreak was fully written up by Shapter seventeen years after its occurrence [12]. Thomas S. Shapter, incidentally, was a well-known Exeter physician. Born in Gibraltar in 1809, he died in London in 1902 at the age of 93. He was a skilled draughtsman, and he had other non-professional interests [13]. Shapter described very well the difficulties which confronted the Local Board of Health, and the deplorable results of the jealousy which existed between it and the Corporation of the Poor. In 1933 I said that I regarded this book as "one of the best descriptions extant of an historical epidemic" [14], and in the following year Mr. R. H. Mottram quoted freely from Shapter's work in opening his chapter on "Town Life and London" in an important collaborative volume [15]. The population of Exeter at that time was 28,242 persons, and there were at least 1,135 cholera cases with 345 deaths. Perhaps the most important part of Shapter's work deals with the various administrative measures which were taken to check the disease, and the attempts which were made to improve the sanitary conditions of the town. The disease first appeared there on July 18, 1832. A local Board of Health had been formed in the City on November 1, 1831, so that the community was as much prepared as it could be at that time. There were great difficulties regarding the provision of an efficient water supply. Until then water for drinking purposes had been obtained from private wells, a few public pumps, the waterworks, and the ancient conduit—the history of which extended back to 1221. By the efforts of Mr. James Golsworthy, the proprietor of the waterworks, fairly satisfactory arrangements were later effected. Shapter gives a very interesting description of the method which was adopted to cleanse the streets. The water was turned on at the fire-plugs, and the stream was dammed in the gutter with coils of straw. Men with wooden shovels then "threw" the water over the road surface. The mean mortality during this epidemic in Exeter was 33%.

In point of time the next important outbreak was that at Bilston in Staffordshire. In 1832 this town had close on 15,000 inhabitants—most of them employed in the furnaces and the mines. A case of cholera occurred on August 3, and within a week there were 150 cases and 36 deaths. The whole outbreak ran its course in seven weeks. The number of cases officially returned to the Central Board of Health was 3,568, and there were 742 deaths. The Rev. W. Leigh, the Incumbent of Bilston, chronicled this outbreak in the following year. His simple record of the events conveys—perhaps more convincingly than impassioned language would have done—the dreadful ordeal of those who lived daily with the dead and themselves feared that they would be the next victims. Writing of August 23 he says: "The condition of Bilston had now become frightful. The pestilence was literally sweeping everything before it, neither age, nor sex, nor station escaping. . . . To describe the consternation of the people is impossible. Manufactories and workshops were closed; business completely at a stand; women seen in a state of distraction running in all directions for medical help for their dying husbands, husbands for their wives, and children for their parents; the hearse conveying the dead to the grave, without intermission either by night or day; those inhabitants who possessed the means quitting their homes, and flying for safety to some

purer atmosphere; those who remained, seeing nothing before them but disease and death [16].” The Rev. Leigh deserves to be remembered and mentioned in the same breath as the Rev. William Mompesson, the plague hero of Eyam in 1665.

The third outbreak to which I shall briefly refer was that at Dumfries [17]. A Board of Health was constituted in that town on March 15, 1832, and active efforts were made to improve the nutrition of the inhabitants and to abate sanitary nuisances. As in Exeter, the domestic and drinking water was provided from the near-by river, and it was sold from door to door by the four water-carriers. Cholera broke out in the town on September 15, 1832, but during the next ten days cases and deaths were not numerous. On the 25th, however, there were 14 new cases and 9 deaths. But the full force of the infection was now to fall on the town. In the succeeding period of six weeks 837 cases were reported officially, and 418 deaths occurred. In the adjacent burgh of Maxwelltown there were 237 cases and 125 deaths. In the combined urban area it is probable that there were at least 630 deaths during these six weeks. In a description of the outbreak it is said that “shops for general business shut at noonday; publicans warned to close their stores at dusk, that the vicious might be hampered in their evil propensities; every vehicle employed in removing family after family to the country; the public schools dismissed; St. Michael’s vacated from the dread of cholera graves, and Divine Service performed in the Courthouse; trade suspended, workshops depopulated, and industrious traders gathered into knots, discussing the fearful extent of the pestilence; many requiring medical aid, and partly from the force of terror alone; every countenance shaded with grief, and a whole community the picture of despair” [18].

We have several firsthand accounts of this outbreak, mainly written by Dr. Archibald Blacklock and Dr. James Grieve, who were in practice in the town in 1832, and who were responsible for the treatment of patients in the cholera hospital. Unfortunately, these letters all date from the years 1848–49 and 1854, and so were written long after the events described. In 1848 Grieve [19] described a peculiar tingling sensation, exactly similar to a slight galvanic shock, which was felt on applying the hand to the skin of a person in the collapsed stage of cholera. Much ink was spilt in endeavours by various persons to establish priority for this observation. More important, Grieve set out in some detail his reasons for believing that cholera is not contagious, and he considered that the diffusion could only be satisfactorily accounted for by admitting the influence of “epidemic causes”. In February 1854 Grieve [20] reverted to the question in a communication dealing with remarks made by W. T. Gairdner in a discussion. From Gairdner’s reply it is evident that there was in Dumfries a strong opinion against the contagiousness of cholera, and that Grieve had been an advocate of this opinion [21]. The old records were then gone over carefully by Blacklock [22] who says that although he had previously felt that, where cholera prevailed, it was the locality and not the sick which had to be feared, the records of the first eight days of the 1832 outbreak had changed his views. He says that “the progress of the disease during the first eight days was, to use the favourite term of Sir Gilbert Blane, more like one communicable by emanations from the human body than one entirely owing to atmospheric influence, or any other influence with which we are acquainted”.

It is unnecessary to refer to the further correspondence which is of some interest from an epidemiological standpoint. During this outbreak four medical men out of 21 practising in the town were attacked, and two of them died [20]. There was apparently no discrimination between the houses of the rich and those of the poor. It is also interesting to read the account of an eyewitness, who was impressed by a dense mass of cloud which hung over the town “like a vast funeral pall”. The verbal picture which he paints is very reminiscent of the plague scenes depicted by some of the great artists: “A dense black canopy enveloped the whole skyey amphitheatre as far as the eye could reach, fringed by a narrow ray of pinky light along the horizon, and the sun rarely shedding a ray upon the towns in which death was so busy” [23].

During the period under discussion the question of the contagiousness of cholera continued to be hotly debated. By “contagion” the idea of actual contact was of course implied. Moir [24] in his important book supported the contagious nature of the disease, but he obviously did not appreciate that the infection does not pass direct. Molison [25] in his account of the cholera at Newcastle held that there are no grounds for believing that the disease is contagious, and as one fact in support of this view he states that he has often sat for half an hour on a patient’s bed, and that on one occasion he had wounded himself with a lancet while bleeding a cholera patient. The problem was often approached in a materialistic spirit. For example, Lizars [26] says: “I consider the pernicious doctrine of contagion has let loose upon the public mind one of the strongest auxiliaries to the propagation of the disease, viz. fear. This is well known, on ordinary occasions, to produce the premonitory symptoms of Cholera, or diarrhœa. The doctrine of contagion hardens the heart—destroys the finer and more amiable feelings of our nature; the kindly affection of

the father for his family is blunted or destroyed; the still stronger link of nature between the mother and her offspring is broken, and she looks on her innocent children as sources of danger. . . . The minds of the vicious are lulled into false security."

During the year 1831 cholera caused the deaths of 21,800 persons in England and Wales, and 9,600 in Scotland. There was a recrudescence in London in 1833, when the metropolis had 1,454 deaths, and also a few scattered minor outbreaks in other parts of the country. But for all practical purposes cholera had burnt itself out, and was not to be seen again in this country until 1848. In Table I are set out the deaths which occurred in the most

TABLE I*.—GREAT BRITAIN. CHOLERA OF 1831-32
Chronological Table to Show Main Cholera Centres

Place	Commencement of epidemic	Termination of epidemic	Total deaths
Sunderland	Oct. 20, 1831	Jan. 9 1832	215
Newcastle	Dec. 7 "	? Summer "	801
Gateshead	? Dec. 25 "	? "	148
Haddington	Dec. 17 "	End Feb. "	65
Tranent	Jan. 18, 1832	? End Feb. "	78
Musselburgh	Jan. 18 "	End Feb. "	202
Edinburgh	End Jan. "	? "	1,065
Leith, &c.	End Jan. "	? "	319
Glasgow	Feb. 9 "	Nov. 11 "	3,166
Paisley	Feb. "	Nov. "	444
Greenock	Feb. "	Nov. "	436
London	Feb. 14 "	Dec. "	5,275
Hull and Goole	Early April "	? "	336
Liverpool	End April "	Nov. "	1,523
Dundee	End April "	? "	512
Manchester	May 17 "	Jan. 1833	706
Salford	May 17 "	Jan. "	216
Leeds	May 28 "	Mid-Nov. 1832	702
Plymouth	June 11 "	Sept. 18 "	{ 702 228 133 } 1,063
Devonport			
East Stonehouse			
Warrington			
Sheffield	June 18 "	Sept. 23 "	168
Nottingham	July 8 "	Oct. 27 "	402
Nottingham	? "	? "	322
Bristol and Clifton	July 11 "	Mid-Nov. "	694
Exeter	July 18 "	End Oct. "	345
Carlisle	Aug. "	? "	265
Bilston	Aug. 4 "	Sept. 18 "	742
Dumfries	Sept. 15 "	Dec. 31 "	{ 418 125 } 543
Maxwelltown			

*Tables I and II have been compiled from various sources. In the case of Table II the data are taken especially from the Registrar-General's reports on cholera. Owing to the frequent occurrence of one or two cholera deaths in an area at intervals of some months before the actual start of the epidemic, the commencing date has generally been taken as that period when initial cases were closely succeeded by others. The difficulty in the diagnosis of sporadic cases seems to warrant this selection, but in any case there must be great difficulty in fixing the commencing date of such epidemics.

important cholera centres in 1832. I have arranged the data—compiled from various sources—chronologically, so as to show the spread of the disease through the country.

The epidemic of 1848-49.—The disease seems to have been conveyed from Hamburg, and it broke out in the Edinburgh district in the beginning of October. In the capital itself there were 448 deaths. On November 11 the disease reached Glasgow, and before it died out it caused 3,800 deaths [27]. The industrial towns of Lanarkshire and Ayrshire were also affected, and Dumfries had an outbreak which was almost as bad as that of 1832. In Dumfries the outbreak started on November 16, and continued until the first week of January 1849. It caused 317 deaths, together with 114 in the adjoining town of Maxwelltown [28]. The combined population of the two towns was then 14,000. Scotland was completely clear of cholera before the disease had obtained a foothold in England. Although there had been a comparatively small number of deaths in London during the autumn of 1848 and the first six months of 1849, it was in July, August and September that the disease really became epidemic in the metropolis. The peak month was September, when there were 6,644 deaths. Other towns which were heavily attacked during the autumn months were Plymouth (830) and Portsmouth (568). Most of the Lancashire cotton towns escaped lightly.

Although the 1832 epidemic caused more fear and appealed more to the popular imagination, the outbreak of 1849 was the most severe that this country has suffered. In England and Wales it caused 53,292 deaths. In Table II I set out data for 1848-49

TABLE II*.—GREAT BRITAIN. CHOLERA OF 1848-49

Chronological Table to Show Approximate Dates of Epidemics in Cholera Centres

Place	Commencement of epidemic	Termination of epidemic	Total deaths
London (a)	Sept. 1848	May 1849	1,017
Edinburgh	Oct. 2 "	Jan. 18 "	448
Glasgow	Nov. 11 "	Mar. 8 "	3,800
Dumfries	Nov. 16 "	First week	317
Maxwelltown }		Jan. "	114
Hamilton	Dec. 24 "	Mar. 7 "	251
Sunderland	Jan. 1, 1849	Nov. 7 "	363
Abergavenny	Jan. 3 "	Nov. 29 "	438
Gateshead	Jan. 8 "	Oct. 31 "	257
South Shields	Feb. 13 "	Nov. 14 "	201
Liverpool and West Derby	May "	Nov. "	5,308
Cardiff	May 13 "	Dec. 7 "	396
Merthyr Tydfil	May 21 "	Nov. 21 "	1,682
Neath	May 21 "	Nov. 10 "	738
Clifton	May 29 "	Dec. 20 "	563
Swansea	May 31 "	Oct. 20 "	262
Bristol	June 1 "	Nov. 2 "	591
Chorlton	June 1 "	Oct. 25 "	280
Portsmouth	June 3 "	? Oct. 5 "	568
Bradford	June 4 "	Dec. 28 "	426
Plymouth	June 9 "	Nov. 8 "	830
Manchester	June 11 "	Nov. 23 "	878
Dewsbury	June 14 "	Nov. 16 "	224
Newcastle-under-Lyme	June 19 "	Oct. 30 "	241
Wigan	June 20 "	Nov. 26 "	503
Salford	June 24 "	Oct. 19 "	237
Plympton St. Mary	June 25 "	Oct. 18 "	151
Wakefield	June 28 "	Dec. 12 "	241
West Ham	June "	Oct. 27 "	134
London (b)	June "	Nov. "	13,584
Stonehouse	July 2 "	Oct. 10 "	171
Leeds	July 6 "	Nov. 28 "	1,439
Hunslet	July 6 "	Nov. 28 "	884
Stockton	July 7 "	Nov. 16 "	248
York	July 9 "	Oct. 14 "	174
Stoke Damerel	July 11 "	Oct. 14 "	721
Hull	Mid-July "	Oct. 30 "	1,834
Wolverhampton, Bilston, &c.	July 17 "	Nov. 13 "	1,365
Gainsborough	July 17 "	Nov. 27 "	246
Stourbridge	July 22 "	Dec. 29 "	314
Pontefract	Aug. 6 "	Dec. 26 "	238
Romford	Mid-Aug. "	End Sept. "	163
Dudley	Aug. 21 "	Dec. 22 "	412
Tynemouth	Oct. 10 "	Nov. 26 "	815
Newcastle-on-Tyne	Oct. "	Nov. 16 "	295

*See footnote to Table I.

similar to those given in Table I. This table brings out the differences between the 1848-49 epidemic and that of 1832. The disease commenced in many different areas almost simultaneously, and, although there had been small numbers of cases in many areas in the early months of 1849, the brunt of the epidemic was borne by most areas in the summer and autumn months.

The epidemic of 1853-54.—This epidemic began with a fatal case in Newcastle on August 30, 1853. The incidence mounted rapidly, and by November 4 there were 1,533 deaths, together with a further 433 deaths in Gateshead. In the following year London had 10,738 deaths; Liverpool (1,084), Dudley (256), and West Ham (124) were also fairly heavily affected, and the small town of Wisbech had 176 deaths. In England and Wales as a whole there were 20,097 deaths in 1854.

The later outbreaks.—During the autumn of 1865 cholera—imported by a new route, from Arabia through Egypt—caused 35 deaths in Southampton. It then appeared at Weymouth, Portland, and Dorchester. Between September 28 and October 31 a small

outbreak with 9 deaths occurred at Theydon Bois in Epping Forest. This outbreak was investigated by Radcliffe, and was shown to have been due to the contents of a faulty cesspool leaking into a well [29]. 1866 was very definitely a cholera year. According to Simon [30] the first case appears to have occurred at Bristol on April 28, and by May 15 cholera was reported in the Mersey centres. The largest number of deaths reported was in London (5,596), and Creighton notes that in the metropolis the disease in 1866 left its old principal seats—Southwark and the parishes on the south of the Thames—and became localized to the East End. In the provinces Liverpool suffered most heavily with 2,122 deaths, and other towns which were relatively badly affected were Swansea, Merthyr Tydfil, Chester and Portsmouth. Although there were few large outbreaks apart from these, cholera was so widespread that it caused 14,378 deaths in England and Wales as a whole [31]. In Scotland there were 1,170 deaths, the places chiefly affected being Edinburgh (154), Dundee (105), Aberdeen (62) and Glasgow (53). A few cholera deaths took place in this country in 1873.

In 1893 there occurred the beginning of what might have been a serious epidemic. In the summer of the previous year the disease was raging in Hamburg, and it will be remembered that while both Hamburg and Altona used water from the River Elbe for drinking purposes, in the case of Altona the water was filtered while in the case of Hamburg no such precaution was taken. Altona escaped the infection completely. During this outbreak, in the period between August 25 and October 18, 1892, 35 cases of cholera reached the shores of Britain, but no residents were affected [32]. In the summer of 1893 the disease was imported again—to the Tyneside ports on June 25, and to Cardiff on July 18 and London on July 20. About the middle of July there was an excess of fatal diarrhœa at Grimsby (Lincs), and cases of true cholera probably occurred from the beginning of August. On August 24 the disease reached Hull, and on September 5, the first fatal case occurred in Rotherham. On September 7 a woman cleaner in the House of Commons had a fatal attack. Grimsby had the greatest number of deaths, 35. Next in order came Hull 12, Ashbourne (Derby) 9, and Cleethorpes 7. Exclusive of ship-borne cases, the total attacks from true cholera in England and Wales in 1893 was 287, and there were 135 deaths. The fatality rate was given by Thorne Thorne—the chief medical officer of the Local Government Board—as 47% [33]. This was the last occasion on which cholera gained a footing in this island.

John Snow and the cause of cholera.—The main interest of the outbreaks of 1849 and of 1854 centred round the mode of spread of cholera. I have already indicated that even as late as 1854 there was widespread disagreement on this question; although many felt that cholera was contagious, no one had succeeded in bringing forward evidence which could not be apparently shot to pieces by the other side. In 1832 John Parkin [34] had suggested that the cause of cholera is a noxious matter or poison which is generated in the earth, and that this finds its way into springs. Parkin also suggested that the water from such springs should be filtered through charcoal before use.

Such was the position in 1849, when John Snow first published a work on this subject. He was then a famous anesthetist, but unknown in the realm of epidemiology, although he had been interested for some time in the problem of cholera. His essay *On the Mode of Communication of Cholera* [35], a pamphlet of thirty-one pages, was published in 1849. He published later articles in the *Medical Times* (1851) and in the *Medical Times and Gazette* (1852). In 1852 he chose the title "On Continuous Molecular Changes" for his oration at the eightieth anniversary of the Medical Society of London. In 1854 Snow seized the opportunity for testing his theories during the occurrence of the Broad Street, St. James's, outbreak in London, and he further conducted a very extensive investigation into the incidence of cholera in the areas supplied by certain London water companies. In the following year he published a very much enlarged edition—now of 162 pages—of his essay [36].

Snow is beginning to receive the attention which he certainly deserves as one of the founders of epidemiology. In this short paper it is not possible to deal fully with his work, but as most of the accounts of his writings concentrate on the second edition of his essay, I propose to say something of Snow's earlier views, as found in his essay of 1849.

Snow begins by asserting his belief in the fact that cholera is propagated by human intercourse. He then goes on to argue that in cholera the alimentary canal is first affected, and he rejects the theory of effluvia, and that of poisoning of the blood in the first instance. A little later appears the illuminating sentence: "The excretions of the sick at once suggest themselves as containing material which, being accidentally swallowed, might attach itself to the mucous membrane of the small intestine, and there multiply itself by the appropriation of surrounding matter, in virtue of molecular changes going on within it, or capable of going on, as soon as it is placed in congenial circumstances." He gives as an analogy the introduction of the ova of intestinal worms into the body; and though the prevailing ignorance of the life-cycle of these parasites made the analogy inaccurate, it was nevertheless in some ways

striking. Snow then suggests that cholera may be widely disseminated by the emptying of sewers into the drinking water of the community, and he gives examples of cholera areas—such as Dumfries, Glasgow, and certain parts of London—in which these conditions existed. He proceeds to build up his case with examples of localized outbreaks in which it could be shown that the drinking water had become polluted with sewage. Then follows a type of argument which he was to develop much more fully in the second edition of his work. Snow pointed out that, of the five districts into which London could be divided, only the south

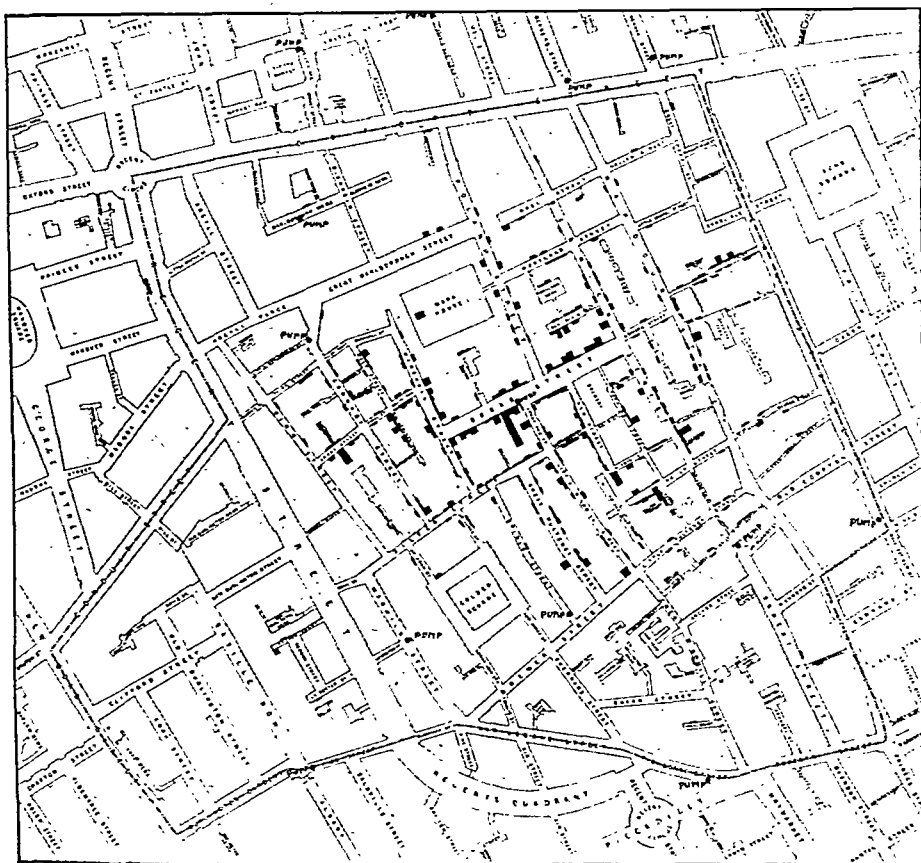


FIG. 1.—Snow's map showing the distribution of the deaths from cholera in the Broad Street (Golden Square) area of London, 1854 (from John Snow, *On Cholera*, London, 1855). The scale of the original map was 30 inches to a mile, and reduction is approximately to one-third.

district was supplied with water taken from the Thames at places where the river was much polluted by sewage. All the other districts obtained their water from points farther upstream, or from the New River or the River Lea. The Chelsea area was an exception. Though it took its water from the Thames only one or two miles above Vauxhall, it was at great pains to filter the water carefully. But the number of cholera deaths in a certain period in the south district—viz. 4,001—was more than that in all the other districts combined. He also makes the significant statement that, when the water had been contaminated, the possibility of the "materia morbi of cholera" being communicated to the inhabitants depended "on whether the water were kept in the reservoirs till this materia morbi settled down or was destroyed; or whether it could be separated by the filtration through gravel and sand, which the water is stated to undergo". Finally, there follows a brilliant anticipation of the germ theory of cholera, which should have served as a beacon to others: "As far as can be judged from analogy", he says, "the poison consists probably of organized particles, extremely small no doubt, but not capable of indefinite division, so long as they retain their properties." Snow summarizes in a few words the preventive measures which

are necessary. Attendants on the sick must wash their hands frequently; water which may contain sewage should not be used for drinking or cooking; or alternatively the water should be filtered or boiled before use. The south and east districts of the metropolis must have a sewage-free water supply.

Snow's second edition of 1855 was really an extension and confirmation of these arguments—but what a confirmation! The episode of the Broad Street Pump is known to many as a name, but only those who have read Snow's text will appreciate the force of the argument. It should be noted that his preface is dated "11 December, 1854", a matter of weeks after the conclusion of the outbreak. The centre of the "cholera field" was the pump in Broad Street, near Golden Square, and the field itself was for practical purposes bounded by Great Marlborough Street, Dean Street, Brewer Street and King Street. In this small area there were over 500 cholera deaths in ten days. Snow called it "the most terrible outbreak of cholera which ever occurred in this kingdom". It began on the night of August 31–September 1. During the first three days the number of persons attacked who subsequently died was 56, 143 and 116 respectively. The mortality would have been very much greater had not most of the population left the area. Snow immediately suspected the water of the Broad Street pump as the cause. On the evening of September 3 he examined that water, but found so little organic impurity that he hesitated to come to a conclusion. Finding, however, that the water showed more evidence of impurity during the next two days, he obtained from the Registrar-General the names of the diseased persons, and he carried out an investigation on the source of the water consumed by each. This enquiry showed that the incidence of cholera was only among persons who drank the water from this pump. On September 7 he had an interview with the Board of Guardians of St. James's parish, and as a result of what he said the pump handle was removed on the following day. The incidence of new cases ceased almost at once. Snow gives an excellent spot map—possibly the first use of a map for this purpose—showing the distribution of cases (fig 1).

There were several features of the outbreak which Snow used in an admirable manner to support his thesis. A workhouse in the area was surrounded by houses in which cholera deaths had occurred, yet there were only five cholera deaths among the 535 inmates: the Broad Street pump was not used as a water supply. A brewery in Broad Street which employed over seventy men had no definite cholera cases: there was no evidence of the men having drunk the water from the suspected pump. A very interesting case was that of a lady who had not been in the Broad Street neighbourhood for months. She preferred the Broad Street pump water, and a cart took a large bottle of it daily to her in her West End residence. She drank the water on Thursday, August 31, was seized with cholera on the Friday and died on the Saturday. A niece who was visiting her also drank the water, was attacked, and died. The pump-well was later examined by an expert, but no direct connexion between sewers and well was found.

Snow then proceeds to discuss the relationship between cholera deaths in various London districts and the water supply to these districts—a practical application of his previous suggestions. In 1854 most of London south of the Thames was supplied by two water companies; the Southwark and Vauxhall Company, which drew its water from a polluted section of the river near Battersea Fields; and the Lambeth Company, which obtained its supply from much farther up the river at Thames Ditton. In a certain area of London the pipes of the two companies ran side by side, and the last house had a choice of two supplies. In 1854, Snow assisted by Dr. J. J. Whiting, visited every house in which a cholera death had occurred and ascertained the identity of the supply used. As a result of this survey Snow showed that, during a seven-week period, the incidence of cholera deaths in houses supplied by the Southwark Company was 315 per 10,000 houses; in those supplied by the Lambeth Company 37 per 10,000; and in the rest of London, 59 per 10,000. This is one of the earliest and most perfect examples of a field investigation in epidemiology. As he says it is "on the grandest scale".

Snow's work is marked by accurate observation, careful reasoning, and logical deduction. Any suggestion that his contribution to the epidemiology of cholera consisted in removing the pump handle in Broad Street is far from the mark.

Social results of the cholera.—Like the Black Death, the cholera epidemics in the nineteenth century in this country, because of the wide dispersion of the infection throughout the land, the suddenness of the outbreak, and the supposed association with housing conditions and filth, had most important social and economic consequences. It is admitted that the 1832 outbreak was the real spark which lit the tinder of the budding philanthropic movement, culminating in the social reforms and the foundation of the official public health movement, seventeen years later. As a stepping-stone to a new age, it is interesting to note that cholera played a direct part in the formation of a great insurance company. The Rev. James Gillman was the son of James Gillman, the Surgeon of Grove House, Highgate, who was the friend and host of Samuel Taylor Coleridge. In 1847 Gillman became Vicar of Holy Trinity,

Lambeth, and there he passed the period of the second cholera epidemic. It is recorded that for three weeks he never returned to his home for fear of carrying the contagion to his family, and during this time he slept on a sofa in the surgery of the parish doctor. His experiences led him to consider the possibility of providing a fund for stricken families on the principle of life insurance. Gillman worked out his scheme with Henry Harben, who was then the secretary of a small and struggling insurance company which was called the Prudential. The new scheme was based on the weekly payment of small sums from one penny upwards, and in 1850 Gillman became the Chairman of the new company. At his death in 1877 the weekly payments amounted to over two million pounds per annum [37].

To sum up, the early Victorians, already beset as they were by the problems which followed in the train of industrial expansion, were confronted during the short space of thirty-odd years with four major epidemics of a new and loathsome disease. These epidemics caused the deaths in England and Wales alone of 21,800 persons in 1832; 53,292 in 1848-49; 20,099 in 1853-54; and 14,378 in 1866. Their success went hand in hand with the foundation of English public health, and with the building up of quarantine and other measures which have kept this island almost inviolate for eighty years.

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Epidemiology of Cholera. [Summary]

By Major-General Sir JOHN TAYLOR, C.I.E., D.S.O., I.M.S. (Retired)

THE main features of the prevalence of cholera are:

- (1) Its continuous existence in permanent endemic form, only in certain limited and fairly well-defined areas of India and the Far East.
- (2) Its repeated extensions in epidemic form, mainly by continuity of land-spread over artificial frontiers, in a vast and highly populated area, comprising India, China and the countries adjoining, without the establishment of true endemicity, and
- (3) Occasional extensions west of India by land and sea routes, which have been infrequent and limited in duration in recent years, recession always occurring with subsequent complete freedom from the disease.

The basic problem of cholera is that of the endemic centres in which alone infection is permanently maintained; but for their existence cholera would presumably die out completely in time. They present a unique feature, for a bacterial disease capable of wide epidemic spread, in their limited and special localization. A combination of factors must exist there that favours the persistence of infection, similar favourable conditions apparently not obtaining in any other part of the world. No full explanation of this special localization has yet been obtained although correlation with certain climatic factors has been shown.

The two major endemic centres are in Lower Bengal and in part of the Yangtze Valley. Other minor centres have been designated but their status in that respect is less well defined. A region would be considered "endemic" in which over a very prolonged period there is a continuous low level of incidence with seasonal rise to epidemic level.

When spread occurs from the endemic areas, or from places previously infected from them, cholera experience is characteristic for each area infected and varies with climatic, geographical and other conditions. Some areas are more favourable than others for the persistence of cholera infection for a considerable period, and when a cycle of infection is occurring such an area will present the same risks of dissemination of infection as the permanent endemic centres. Their significance is not, however, the same as the centres that form the permanent reservoirs of infection.

There is no evidence that recrudescence of cholera can occur in the sense that a fresh outbreak can develop after a prolonged period of freedom from human cases without a fresh introduction of infection. Extensive field investigations in India, carried out in both endemic and epidemic areas have failed to show the presence of the vibrio except in close relation to the human case of cholera; the persistence of the vibrio in the human intestine and in water has been found to be of limited duration. The general indication obtained from recent investigations is that infection is maintained by the chain of human cases, convalescents and close contacts excreting the vibrio with, in some cases, short periods of intermediacy in water.

The problem of control in Asia.—The main spread of cholera in East Asia occurs by extension of infection over artificial land frontiers of countries and provinces in continuity with the endemic centres, or areas infected by them, under conditions in which quarantine control measures cannot be applied effectively. The existence of an endemic centre is a permanent source of danger to neighbouring areas which are put at a continuous risk of an epidemic disease against which they are not in a position to take primary action. The obvious policy to adopt for the prevention of cholera is to concentrate the main measures in the centres in which infection is permanently maintained, with the object of eliminating the source. The Governments of territories in which endemic centres are situated have a responsibility in the matter towards their neighbours, and to world health in general, that should be recognized. The matter might suitably come within the purview of the World Health Organization (WHO) with a view to assistance in investigation of the conditions in some of the endemic areas and of help in co-ordination of measures, where this help may be required.

The control of spread to the West.—In successive pandemics of cholera three main lines of extension have been recognized:

- (1) From India through Afghanistan and Iran to the Caspian and Caucasus and on to Russia.
- (2) By the Persian Gulf to Iraq and on to Syria and Turkey and the Mediterranean, and
- (3) By the Red Sea route to Egypt.

Subsequent spread resulted in scattered incidence, often with considerable mortality, in many parts of Europe and infection was even carried to the American Continent on occasions.

By the first of these routes, the long land route from India, infection has not been carried to Egypt for many years. The route does not at the present time constitute a major danger, but should be watched. Iraq has been infected eight times in the present century by sea traffic from India, the last outbreak being in 1931. Active measures were required to prevent onward land spread to Syria and Turkey on those occasions. With improving communications the risk of spread in future may increase. The short sea journey from India to the Persian Gulf ports is a factor facilitating introduction of cholera to Iraq. The main safeguard will be the strict enforcement of quarantine measures in relation to the risk that exists. This line of introduction to the West is definitely important and will require to be watched carefully.

On the third route by the Red Sea the danger at one time was mainly of introduction of cholera to Egypt by the pilgrims returning from the Hedjaz by land or by a short sea voyage at times when the Pilgrimage to Mecca was infected. Successive severe epidemics were caused in Egypt in this way, the last occurring in 1902, although the Pilgrimage was also affected in 1907, 1908, 1911 and 1912. Cholera has not occurred on the Pilgrimage since 1912. This prolonged freedom from cholera is a striking example of the value of quarantine measures designed to meet special circumstances and risks, and full reliance on them has been justified. Important points in present practice are: (a) the detention of the pilgrims at the port of embarkation in India for five days before proceeding on board ship, and (b) the subsequent call at the quarantine station at Kameran on entering the Red Sea and before proceeding to Jeddah for final disembarkation.

The risks that may exist of importation of cholera to Egypt by the direct sea route from India or the Far East may be considered in relation both to the actual cholera case and to the individual, either a convalescent or a contact, who may continue to excrete the vibrio in his stools. On the latter point the question of the cholera carrier arises.

It is not of course possible to assert dogmatically that occasional cases of prolonged excretion do not occur but there is no evidence that individuals have been responsible for the production of successive groups of cholera cases for long periods after their first infection. In this respect the chronic carrier state has not been shown to exist in cholera in the way it does in typhoid. The epidemiological characteristics of cholera would be widely different from those that have been observed if the chronic carrier acted as a definite agent in transmission. From a fresh study of the period of excretion of the vibrio by cholera convalescents and contacts which was undertaken in India in 1939 it would appear to be five days in the majority of cases, but the vibrios may still be present up to two weeks, or slightly longer. These observations may be employed in assessing the risks of carriage of infection in the course of the long sea route from India to Suez, the duration of which is over seven days.

A person incubating cholera at the time of embarkation in India would develop cholera on board ship before reaching Suez, the incubation period being taken as up to five days. Dr. Morgan and Dr. Balfour Kirk have obtained for me information of such occurrences in the course of voyages from India, Saigon and Abadan and vessels have arrived at Suez with cases on board necessitating quarantine action. Provided the occurrence is recognized or suspected the appropriate quarantine procedure should provide adequate protection against the introduction of infection. In the case of convalescents and contacts who may excrete the vibrio in their stools, the period of major risk due to persistence of infection acquired before embarkation will be passed before completing the voyage to Suez. The maintenance of infection on board ship by the occurrence of a mild case or two, not diagnosed or suspected, is a possibility to be kept in mind; infection might be introduced in this way. The protection against this will be the effective action of the quarantine staff in the detection of any suspicious occurrences.

A new risk of the spread of cholera has been introduced by modern developments in air travel, but it will usually be easy to trace the movements of passengers and any possible contacts with cholera. The time factor in regard to infectivity that I have mentioned in relation to sea travel will also apply in the case of air travel. The main risk would be the development of a clinical attack of cholera by a passenger after departure from the airport, in an area where conditions are favourable for the establishment of infection and subsequent spread. It is unlikely that a very recent convalescent would be permitted to travel but a positive contact might arrive by plane in an infective condition.

So far we have no definite information on how infection was introduced to Egypt at a time when the disease had not been reported as occurring in any other country west of India. Air or sea carriage from the East must be presumed.

Anti-cholera inoculation may usefully be employed in quarantine practice, with adequate certification of performance. Statistical evidence of its value has been somewhat limited up to now, but a report has just been published in India on the results of a statistical examination of its prophylactic value, based on very large figures. The report has not yet been received

in this country but it is understood that definite evidence of a considerable degree of protection is presented. The possession of an inoculation certificate does of course ensure complete freedom from risk.

Bacteriological and Immunological Aspects of Cholera.

[Summary]

By P. BRUCE WHITE, B.Sc., F.R.S.

IN the nineteen-thirties an international reinvestigation of *Vibrio cholerae*, its serology and relation to cholera, was undertaken, which culminated in the extensive field trials and investigations which Sir John Taylor organized in India.

At this time two items of information were waiting general application to laboratory practice. On the one hand, first Balteanu, then Shousha, Abdoosh and Gohar in succession had successfully applied to the vibrio the receptor analysis methods of Weil and Felix and on the other Kabeshima and a series of later Japanese observers had pointed out that the classic vibrio occurred in the closely related but serologically different forms which they termed the Original, Intermediate, and Variant types.

As participants in the International Investigation of 1934-35 Dr. A. D. Gardner and I confirmed in detail the findings of all these workers on an extended series of vibrio strains of varied provenance, added certain novelties of our own and were able to present the whole in one picture and to offer some suggestions as to the best methods of utilizing the newer knowledge in practice.

The essential points established were the relative specificity of the O agglutination reaction and the existence of Inaba and Ogawa subtypes of cholera and El Tor vibrios. The reason for many past discrepancies in the identification of cultures was that those who had read their agglutination tests early had recorded the specific reactions of the O antigen; those who had read them late registered the wide range of H non-specificity.

Gardner with his Indian colleague, Venkatraman, armed with the new knowledge, began what Greig had formerly attempted, a serological classification of the vibrio world. They succeeded in classifying the majority of the available vibrio strains from cholera patients, healthy subjects and water sources into six O agglutination groups of which *V. cholerae* and *V. El Tor* with their subtypes formed Group I.

At a meeting arranged by the Ministry of Health at which Sir John Taylor was present Dr. Gardner and I took occasion to urge that a pure O anti-cholera serum, or preferably the separate O antisera of the Inaba and Ogawa types, formed the proper reagent or reagents for the recognition of *V. cholerae*. The result was that at Sir John's request I undertook to prepare, not pure O antisera, but pure O antigens, which might be supplied to India and all others interested for the local preparation of valid diagnostic antisera. Dr. Gardner undertook to check the properties of my vaccines—which we rather flamboyantly called "standard O antigens"—to issue them as required from the Standards Laboratory, Oxford, and to collect and analyse any reports that might come in. From that time the O-Inaba and O-Ogawa antigens have been dispensed as requested from the original bulk preparations amounting in each case to about an ounce of dried, alcohol-extracted, steam-treated, ether-washed powder of which the bulk still remains in hand.

It is sufficient to say that, whatever other problems remained unsolved, the extensive trials which Sir John Taylor organized in India completely vindicated the hope that the sera raised against these and like antigens would give to the search for *V. cholerae* a precision hitherto lacking. The results have been set out in detail in the *Indian Journal of Medical Research*, 35, 3, July 1947.

At their first differentiation there was some suspicion that the Original or Inaba type of *V. cholerae* might be the organism of epidemic cholera, the Variant or Ogawa type that associated with the sporadic case. This was not supported by later Japanese observations; nevertheless there clung the suggestion that the Ogawa type might be a *mitis* form responsible for outbreaks of relatively mild disease. There does not seem to be any evidence either from the Japanese or later Indian investigations that this is really the case. The doctrine grew up that the type concerned in any epidemic was fixed though there might be mixed epidemics due to collateral spread of more than one type of the vibrio. For instance in the great Shanghai epidemic of 1932, 12 of 15 strains isolated in the early phase and 48 of 53 strains isolated in the later phase were of the Hikojima or middle type, the remainder being Ogawa. It was argued that the epidemic had kept its balance and Kuroya and Ono wrote of the "inalterable character of the serological types of vibrios". In India, where Sir John arranged for the distribution of type monospecific antisera, it seemed that the Inaba

and Ogawa types each had their more or less distinct zones of influence though each made occasional epidemic incursions into the territory of the other; in some outbreaks the singleness of the epidemic type seemed absolute, in others a few cases due to the sister type were encountered; some outbreaks were frankly mixed.

In his first description of the Original and Variant subtypes Kabeshima had stated that they were transmutable and he gave an instance in which the Variant type had yielded the Original type during transfer in media containing its homologous antiserum. Later workers, probably believing that in 1917 Kabeshima could not possibly have known enough about vibrio serology to understand his observations, have brushed this statement aside and have assumed the distinctness and fixity of the subtypes. I myself made several attempts to check his view without success, obtaining only, from the type cultures exposed to their antisera, the salt-agglutinable "rough" variants in which the O specificity of the organism is lost. But during a recent visit to India, Dr. D. L. Shrivastava, Biochemist to the I.R.F.A. Cholera Inquiry, and I applied to the type strains, not their full sera, but their monospecific antisera from which the common antibody had been removed, so focusing the serous influence on the type-specific antigen. Without difficulty we converted every one of 13 Ogawa type cholera and El Tor vibrios to the Inaba persuasion; and though we were unable so to alter Inaba type strains to the Ogawa type we found it possible to induce 4 of 8 strains of the Intermediate type, stemming from an outbreak in Calcutta, to make this change. Quite clearly the types are not separate species or subspecies but phases of a single species—something like the specific and non-specific phases of the Salmonella. Incidentally the instance is interesting from the point of view of basic serology in that, while such changes and the modifying influence of serum are well known in the case of the presumably protein flagella antigens, this would seem to be the first in which they have been observed to affect the polysaccharide-lipoid O complex.

I rather suspected that when platings from cholera cases were carefully examined we should find that in quite a number more than one type would be found as a result of spontaneous variation during pathogenicity. In the careful examination of about 100 cases of the spring epidemic at Calcutta, shared equally between the Ogawa and Inaba types we were, however, unable to discover a single instance of "mixed" infection. What bearing the now known transmutability of the types has on the importance to be attached to their differentiation in the field and what bearing it has on the proper composition of cholera vaccine it is difficult to say.

To pass on: following up Gardner and Venkatraman's classification by O groups and Heiberg's classification based on fermentation and non-fermentation of mannose, arabinose, and saccharose, and once more applying the cholera red and V.-P. tests of the old masters, Sir John Taylor and his co-workers were able:

(a) To show that a vibrio which ferments mannose and saccharose but not arabinose and is at the same time cholera red positive and V.-P. negative and non-hæmolytic is in all probability a true cholera vibrio of O group 1.

(b) To classify 311 of 558 vibrio strains inagglutinable with O group 1 serum and drawn from cholera cases, healthy people and water sources into 33 O groups, so making it possible to argue the role of these in the causation of cholera by consideration of the origins of their several component strains. The conclusion reached by Sir John Taylor in assessing the collected results of this and other series of examinations was that, with one possible exception, no case for the cholerigenic activity of any of these could be made out.

In comment on this conclusion, to which I cannot but in general concur, it must be admitted that in India many experienced cholera workers are by no means so convinced, and for one reason or another cling to the view that vibrios other than *V. cholerae* may from time to time contribute to cholera.

Dr. Melville Mackenzie described the measures taken to deal with the Egyptian outbreak on the international level. The Interim Commission of the World Health Organization offered help to the Egyptian Government and on their request undertook to purchase cholera vaccine for them. This method of purchase had been satisfactory but in the absence of any standards the Egyptian authorities had been asked to test the antigenic efficacy of the vaccines received. The Commission's Expert Committee on Quarantine held an emergency meeting at which the Egyptian Under-Secretary of State for Quarantine gave an account of the epidemic. The Committee were impressed by the extent and thoroughness of the steps taken by the Egyptian authorities. It appeared that some countries had imposed restrictions on travellers from Egypt which greatly exceeded the provisions of the International Sanitary Code. These measures were inspired by fears which largely arose from insufficient knowledge of the true epidemic situation; in order to allay them infected countries should provide prompt information to the WHO for transmission to national

health authorities. The Committee gave advice on precautions against the spread of cholera in aircraft by infected water, passengers or flies.

In England and Wales all M.O.s.H. were informed of the occurrence of the outbreak and of its course. Advice was given about dealing with ships and aircraft arriving from an infected port. Travellers arriving by air were not kept under surveillance until the occurrence of suspected cases in Italy and Australia when it was applied to those who had, in the five days before arrival, slept one or more nights in Egypt. Cholera inoculation prior to arrival was not insisted upon. Other countries had done so and in some countries inoculated persons had been exempted from surveillance but this seemed to place excessive confidence in the protective value of the vaccine. The Ministry of Transport had warned ships calling at Egyptian ports that as far as possible they should not allow those on board to land or take on water, fresh fruit or vegetables. The import of baled cotton, sacked rice, rags and dates had not been prohibited.

Arrangements had been made for Sir John Taylor and Mr. Bruce White to visit Egypt on behalf of the Ministry of Health and the Medical Research Council in order to study the results of the use of sulpha drugs and the value of DDT spraying and to carry out researches on the cholera vibrio. There was need for scientific investigation of the length of the cholera vibrio's viability (1) on flies particularly when carried by aircraft, (2) in sewage both crude and during treatment, and (3) on fresh fruit and other commodities. The Expert Committee on Quarantine was interested in these questions and in the standardization of cholera vaccine and the Commission had been offered some 6,000,000 French francs by the Office International d'Hygiène Publique for epidemiological research with cholera as a first objective. Medical supplies to the value of £5,000 were being flown to Egypt within the next few days.

Sir Leonard Rogers showed maps illustrating the spread of cholera epidemics from India to Europe during the nineteenth century. With regard to the present outlook the speaker said that cholera incidence might be expected to decline in Egypt during the latter part of November and to die down in December and January, but there was a serious danger of its breaking out again in that country in 1948 in the spring or early summer with rising temperature and absolute humidity, but the geographical conditions were favourable to its control by modern methods and to the prevention of its spread over South Europe such as occurred in 1883-84. There was, he thought, grave danger of the present epidemic in the troubled and chaotic conditions of the Punjab being carried by the invading North-West Frontier tribes to Afghanistan, and recurring there in the spring of 1948 with spread by the usual overland route to Southern Russia, whose very lengthy land frontier would be most difficult to protect against invasion by the disease in spite of medical advances in Soviet Russia. Overcrowding in Russian towns would be favourable to the spread of cholera if it gained a firm foothold in that vast country. That line of spread might prove to be more dangerous than from Egypt, but it was to be hoped that modern medical science would prove equal to the occasion.

Lieut.-General Sir Bennett Hance observed that in checking the epidemic in Egypt the principles of attack were the same as those holding in India—namely attention to environmental hygiene and inoculation.

In rural India at any rate attention to environmental hygiene could be summed up in the disinfection of water supplies since, outside large towns or organized cholera camps, nothing like efficient conservancy or protection of food supplies was possible. Where piped water supplies or wells existed disinfection by chlorination was comparatively simple, but where, as in parts of India, the water supply was the village "tank" or, as in Egypt, a sweet water canal, such measures became difficult or impossible. It followed, therefore, that all the more reliance would have to be placed upon inoculation, and it was satisfactory to know that, at last, a controlled and statistically authoritative evaluation of the efficacy of inoculation was available (*see Ind. J. med. Res.*, 35, 3, July 1947, by R. Adisesan, C. G. Pandit and K. V. Venkatraman). This would appear to establish the efficacy of the measure upon which doubts had been thrown by the various authorities. Such experience as the speaker had had in handling outbreaks of cholera had certainly tended to confirm the efficacy of the measure and, in consequence, he personally had never doubted it; but the confirmatory evidence of the survey referred to was most satisfactory. A combination of environmental hygiene and inoculation had removed most of the dangers of the great Pilgrimages in India and, in areas where the water supply was "tanks", the speaker personally knew of only one method of holding the spread of cholera and that was "at the point of the needle".

Section of Pædiatrics

President—W. G. WYLLIE, M.D., F.R.C.P.

[November 28, 1947]

DISCUSSION ON THE PLACE OF CHILD GUIDANCE IN THE NEW HEALTH SERVICE

Dr. Ian Skottowe, (Royal Bucks Hospital): *A case for integration.*—The Child Guidance Movement has been active, in organized form, in this country continuously since 1929. It has come to embrace practically the whole of the psychiatry of childhood, except gross mental deficiency. When the movement began, enthusiasm for dynamic psychopathology was keen and widespread, and this approach was blended with an attack upon social and educational factors in the psychiatric disorders of childhood. In this way the traditional team of psychiatrist, psychiatric social worker and educational psychologist came into being, and there was a tendency for child guidance to become highly specialized and somewhat isolated, not only from general medicine, but also from general psychiatry.

In the intervening years knowledge has been gained and viewpoints have broadened so that those who deal with the psychiatric disorders of children must take into account a wider range of specialties than is implied by dynamic psychopathology alone. The relevance of organic neurology, special disabilities affecting the speech function, metabolic disorders, endocrine dyscrasias and nutritional problems is important. More recently, electroencephalography, audiometry and the assessment of motor skills have received close attention.

On these grounds, there is a strong argument in favour of integrating child guidance with the New Health Service, and offering it as a customer service to education authorities, since the latter, although they have an indispensable contribution to make, could not, within the school medical services, provide all the facilities that the maladjusted child may need, without excessive duplication. Other advantages of this integration are that it diminishes the chance of unfortunate results arising from too early and too excessive specialism within a specialty; it brings the family doctor right into the picture, for it is often he who is first consulted by the parents; and it provides facilities for psychiatric interviews with the parents themselves—often an important part of the treatment of the child.

Clinical features.—A survey was made of a random sample of 100 consecutive patients up to 16 years of age, seen at the Psychiatric Department of the Royal Buckinghamshire Hospital, Aylesbury. Patients were drawn mainly from the static population of the district, evenly divided between rural and urban elements. 64 of the children were referred by their family doctors; 17 by other hospital departments (i.e. the presenting picture was that of an illness other than a psychiatric one); 31 of the children were between 14 and 16 years of age. The clinical forms of illness or maladjustment included: anxiety states, 24; behaviour problems and habit disorders, 40 (8 enuretics); special disabilities, 17; mental defect, 14, + 4 others of subnormal intelligence (10 of these were first diagnosed in the 14 to 16 age-group); depressive syndromes, 4; toxic-exhaustive states, 3; schizophrenia, 3. 33 of the patients had somatic disorders, with varying degrees of relevance to the psychiatric syndrome, which needed the attention of specialists in other branches of medicine; and a further 9 had symptoms requiring somatic investigation. 90 of the patients were treated as out-patients; 10 needed residential treatment (3 mental hospital, 2 general hospital, 5 in a hostel, or residential special school); 19 of them needed the services of an educational psychologist, and 18 needed social service in its therapeutic, as contrasted with its investigational, aspects. It is suggested that the features of this clinical material clearly warrant general hospital facilities being available for maladjusted children.

Practical proposals.—The Joint Memorandum of the Royal College of Physicians, the British Medical Association and the Royal Medico-Psychological Association (1945), and Blacker's Survey (1946) suggest that the unified form of child guidance clinic of the past education respectively, but sharing at the clinical level a common technical staff. There would be a child guidance centre, managed by the education authority, where an educational psychologist would do the preliminary grading of children's aptitudes and abilities. Any child who presented active symptoms, or who was clearly maladjusted, would be referred to the school medical officer, and through him a psychiatrist would be available as a consultant at the centre. Should it be thought that the child could more suitably be treated at the psychiatric department of a general or special hospital, he could then, on the psychiatrist's advice, be referred there. This branch of the psychiatric department of the general hospital would be known as the child psychiatric clinic and, ordinarily, it would be the same psychiatrists who would attend at both places—the centre and the clinic. Should it happen that a child was referred in the first instance to the clinic, before his difficulties had been spotted at the centre, and should the psychiatrist at the clinic consider that educational factors were important in treatment—for instance, the services of an educational psychologist, or administrative problems, such as change of school—he should then approach the education authorities through the school medical officer. Thus there would be two-way collaboration, which would preserve continuity of treatment for the child throughout. A psychiatric social worker should be attached to the clinic rather than to the centre.

It has been said that these proposals involve dual administration, but this is not in fact so. Dual administration would mean having two people in charge of one organization. What is proposed here is that each should be in charge of his own, and that there should be easy inter-availability at the school level, the school medical officer being the administrative go-between.

Above all, the management of the child who needs psychiatric attention should be effected under the guidance of a suitable psychiatrist from the start, through whatever channel help may be sought; so long as this aim is realized, it matters little who is in administrative charge of the centres or clinics in which the psychiatrist works. It should be no more difficult for a doctor from the health services to act as a consultant to the child guidance centre, without being in charge of it, than it would be for him to be a consultant to an old men's home, an insurance company or one of the fighting services, nor should there be any difficulty about a psychologist from the education authority being available to a health organization, if he or she has a part to play in the treatment of a patient.

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Dr. A. A. E. Newth (Nottingham Education Committee): Child guidance has two main objects—the diagnosis and treatment of maladjustments in children, and prevention and treatment through parents, teachers and others who have the care of children.

The majority of maladjusted children are basically normal. Psychosis is rare in children. The potentially psychotic child may be maladjusted, but the vast majority of maladjusted children are not at all psychotic nor are they ever in any danger of becoming psychotic.

The approach should therefore be not from the adult suffering from the severer forms of psychosis towards the child who is seriously disturbed, but from the normal child towards the one who has become less well balanced.

The medico-psychological or even purely medical aspects of many of the cases cannot be ignored and accurate medical diagnosis is essential. In treatment, also, the deep psychotherapeutic practices sometimes involved are dangerous without the supervision of a medical psychiatrist.

Some of the plans suggested during the last few years involved the taking over of the whole work by a mental health service catering for persons of all ages and of all grades of mental efficiency and deficiency and of all kinds of mental disturbance from the milder forms of maladjustment in children to the grossest forms of incurable psychosis and dementia in adults.

Is such planning really sound? Is the physician preoccupied with the more dramatic forms of mental disturbance and disease in adults as seen in mental hospitals likely to be sympathetic with the almost normal misbehaviour and psychological mishaps and educational misfits of children? Will not parents, teachers and doctors be reluctant to refer cases to a clinic which they suspect is even remotely connected with mental deficiency or insanity?

Dr. Blacker has clearly shown that the adult mental health service is unable to cope with the large amount of neurosis that exists to-day. It seems scarcely logical to overburden it still further with maladjusted children.

It has been suggested as a corollary that there should be child guidance clinics within the educational system run by educational psychologists who are to be entrusted with the diagnosis and treatment of those children not showing *prima facie* signs of mental instability. Such a policy is open to the strongest criticism as it places on lay psychologists a responsibility with which they should not be burdened however capable they may be.

Many education authorities like my own have established child guidance centres under the supervision of the school medical officer with a team comprising the educational psychologist, the psychiatric social worker and the child psychiatrist, under the technical supervision of the last-named, with lay psychotherapists, educational therapists and speech therapists, in a clinic separate from, but close to, the main school health clinic. The educational psychologists spend a great proportion of their time in the schools in contact with the teachers dealing with other educational problems. Thus the closest liaison is maintained with both the medical and educational aspects of the work.

The educationally subnormal child for the special school and the ineducable mentally defective are kept out of the scheme, and the occasional psychotic is referred to the mental hospital physician.

If, as is not infrequently the case, the seriously neurotic or even perhaps psychotic parent needs treatment she is referred to the mental hospital physician, although help can be given to the worried parent in the clinic by the psychiatric social worker.

Hostels are available for those children who cannot be suitably treated at home; a lien on several hostels is invaluable so that there may be a choice for varying types of cases.

For the child who is ailing physically, the whole gamut of the school health service is available including residential special schools where prolonged physical treatment can be given.

In my area a large proportion of the cases are referred by the teachers who are the first to observe unusual symptoms in school or to receive complaints from parents of difficulties in the home. In other types of clinics there would be a tendency for cases to be referred by doctors outside the school health service only when the condition had become well established.

The large children's or specialized hospitals are called upon for accurate neurological or other examinations or in-patient observation that prove to be occasionally necessary.

As for the much-needed staffs, the training of these is supplied by the teaching child guidance clinics of London and elsewhere.

It is to be hoped that the family doctor will himself be willing in the future to play a greater part in the prevention of maladjustments in the family and their treatment in the early stages.

The aims of the Education Act are to provide a complete service for children at "all ages, abilities and aptitudes", and child guidance is an essential part of such a Child Health Service, foreshadowed by Sir Wilson Jameson to be a part of the National Health Service.

Dr. E. M. Creak: Blacker, in his book, "Neurosis and the Mental Health Services", outlining his conception of plans to deal with children's problems, discusses the provision of educational clinics to deal with the simple problems shown mainly in relation to school, and child psychiatric clinics attached to a hospital and under the control of the Health authority.

While this implies that educational problems may be simpler to deal with than others, such is not necessarily the case, and it is impossible to judge accurately the "difficulty" of a child's problem, either on the basis of the manifest severity of symptoms, or by observing their precise nature. Since prediction is so uncertain, it seems important that every child guidance clinic should have an experienced psychiatrist available. The separation of problems into "educational" and "psychiatric" is unsound, and the team of psychiatrist, psychologist and social worker seems likely still to give the best approach for the initial survey. It would, however, be undesirable that the new National Health Service should attempt to cover the whole field of child psychiatry with a uniform type of clinic.

Among others the pædiatric hospital will get its full share of psychiatric work, more especially since nervousness in children is so commonly shown by a physical manifestation. The pædiatrician will tend to be consulted in the problems of infancy, such as feeding difficulties, and, even at this early stage, the mother is herself often aware that she needs psychological rather than physical help in establishing normal habits, and a secure adjustment during early childhood.

It is to the pædiatric hospital again, rather than to the psychiatric, that the more severe disorders of early childhood present themselves. Such children often give a history of

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of social and vital statistical data for Willesden with those of London as a whole show that this borough can be regarded as typifying the metropolitan population.

When the dates of death and the homes of the fatal cases were examined, it was found that they were not randomly distributed in time or place. They tended to be aggregated in both ways: about one-quarter of the deaths happened in 17 of the whole 468 weeks reviewed, and they occurred with unexpected frequency in near-by houses or in short streets. From both standpoints there was evidence of epidemic association, and it seems reasonable to believe that some local common factor, of which the most likely is some specific infective agent, is responsible for the frequent occurrence of such individually small, but numerous, focal outbreaks as those recorded in Willesden.

Assuming that an important fraction of the deaths from infantile enteritis have an infectious aetiology, I shall now review briefly the relative importance of the three forms—neonatal diarrhoea, parenteral infections and infectious enteritis—in London in recent years.

The form known as "neonatal diarrhoea" was first recognized by Frant in New York in 1937, and since then numerous institutional outbreaks have been recorded. In New York, Frant found that while the mortality of infants under 1 year from enteritis had been falling steadily, that of infants under 1 month had been rising. In London, the same reciprocal trends are now becoming apparent. In the decade 1930–39, about one in twenty of the deaths of infants under 1 year took place in the first four weeks of life. In 1940, it rose to one in six and has since remained high. The change in proportion can only be partly accounted for by the fall in enteritis mortality between the ages of 4 weeks and 1 year. It has also been brought about by a rise in mortality of infants under four weeks—which is now substantially higher than before the war—a possible result of the increase in institutional midwifery in recent years. It thus seems likely that the importance of neonatal diarrhoea is increasing both absolutely and relatively, but it has had little effect yet on the domiciliary enteritis of a suburban area.

The parenteral lesions that have been most often incriminated as possible antecedents of enteritis have been in the upper respiratory tract and its associated sinuses. In Smellie's series, one-quarter had otitis media or mastoiditis and one-seventh bronchitis or pneumonia, at the time of admission to hospital. In Campbell and Cunningham's series, the incidence of tonsillitis, laryngitis, bronchitis and pneumonia was much the same, but otitis media was much less common. There is thus ample evidence for the frequent association of such parenteral infections with enteritis—the question is: Which condition is to be regarded as primary?

A further reason for interest in the possible connexion between parenteral infections and enteritis is the rise in enteritis mortality in the first quarter of the year in London in recent years. Twenty-five years ago the mortality for the quarter January to March—the season of maximal respiratory infections—was 1·7 per 1,000 births. Just before the war, it had risen to 3·6 per 1,000—more than twice its former figure. Yet in spite of this rise there seem to be several reasons for doubting whether these parenteral lesions take a very important place in the aetiology of enteritis. Campbell and Cunningham examined their patients on admission and at intervals subsequently for evidence of parenteral infection. Amongst nearly 300 dehydrated infants, only about one-quarter had such infections at their first examination, but nearly the same fraction developed otitis media or bronchopneumonia after the symptoms of enteritis had become well established. Wishart and Smellie also have drawn attention to the frequency with which infants suffering from enteritis develop otitis media while under care in hospital. Such observations lessen the force of the evidence—much of it derived from post-mortem room studies—upon which the idea of parenteral enteritis was originally based.

In the records for infantile enteritis in Willesden, supplementary information upon concurrent pathological conditions was frequently available. Of the 285 deaths from enteritis, only 43 had records of accompanying infections of their respiratory tracts, and these cases were distributed almost uniformly in all the quarters of the year.

Lastly, when the Registrar-General's data for the decade 1929–38 are examined, there is no tendency for the mortality from infantile enteritis in London to be unduly raised in the years of raised mortality from bronchopneumonia, measles or pertussis. Secondary enteritis is a not uncommon complication of measles, so that in measles years a small, but probably very small, fraction of the deaths recorded as due to enteritis should probably have been more correctly ascribed to measles.

Smellie's "Infectious Enteritis"—the unknown enteral infection without demonstrable pathogenic organisms—is the third of the major forms. Hitherto much of the emphasis upon the infectious nature of enteritis has come from clinical experience in institutions for the care of young children. Such outbreaks, often caused by members of the dysentery group of bacteria, have provided a large proportion of all nosocomial diseases. Valuable though these institutional studies are, they must be carefully distinguished from our present

normal development for the first year or more. Soon however an apparent regression, which is often more a failure to progress, sets in. By the time they reach school age they have usually become unable to take part in normal education. They therefore do not find their way to educational clinics, where the psychotic picture would be distinguished from mental defect, but often go into institutions for mental defect because of their complete inability to adapt socially. The help given by expert psychological testing may be required at the pre-school age to differentiate these from each other, and again from children who are neither ill, nor retarded, but who appear so through sense deprivation, particularly deafness, occurring at an early age.

The general field of psychosomatic medicine increases its range, and nowhere is this more true than in pædiatrics, where asthma, cyclical vomiting, enuresis and other habit disorders abound. Nor can the psychological aspect of chronic physical illness be lightly dismissed. It has been observed by Bowlby and others (Bowlby, J., *Int. J. Psychoan.*, 25, Pts. 1 to 4, 1944) that prolonged hospitalization at an early age is very prone to produce severe affective disorders in later age, in some cases predisposing to a schizoid withdrawal, in others frankly delinquent, anti-social conduct. Nevertheless, recurrences of a physical illness may often be precipitated by the maladjustment resulting from long periods away from normal surroundings of family and school. Here, the value of a psychiatric investigation will be in the direction of avoiding or anticipating breakdown in two directions.

First, during the child's stay in hospital, much can be done to minimize those factors tending to produce either a withdrawal into fantasy life or an unnatural dependence on the protective aspect of hospital care. Secondly, the extremes of fear and rage, love and hate, can be both understood and avoided by personnel trained in a real knowledge of normal developments in the young child.

Such understanding should form part of the training of every pædiatrician, and of nurses having the care of sick children. Not only must they be aware of the normal capacities appropriate to different ages, but they must acquire an understanding of the dynamic factors which are present in the common disorders, and in deviations from the normal.

It is difficult to see how this can be done unless a department of child psychiatry exists as a normal working department of the children's hospital. There the psychological angle of an apparently wholly medical problem can be seen, studied, and treated. Both diagnosis and therapy must be available in order that ordinary mechanisms of psychological disorder may be understood.

[January 23, 1948]

DISCUSSION: THE ÆTIOLOGY OF INFANTILE ENTERITIS

Professor G. Payling Wright (Department of Pathology, Guy's Hospital): Until some years after the 1914-18 war, infantile enteritis mortality was dominated by epidemics of summer diarrhoea which reached their peaks in the late summer. These seasonal epidemics have not taken place in London for twenty years, and have almost disappeared also from other large English cities. Although this formerly preponderating component of infantile enteritis is no longer recognizable in the Returns of Infectious Diseases there still remain many deaths in this category of the Registrar-General's Reports. In the County of London, between 1934 and 1938, they averaged more than 700 annually, and even in the war years, when births in London were much reduced, they remained between 300 and 400 yearly.

There is general agreement that epidemiologists use the term "infantile enteritis" to cover several diseases of different ætiology. In some cases the enteritis seems to be primary, in others it is secondary to disease processes elsewhere in the body. In some infants it seems to arise from dietetic causes, in others an infective agent, such as a dysentery bacillus, provokes its onset. Smellie, in his study of enteritis in Birmingham, classified his cases into four categories: "Infective", "Infectious", "Parenteral" and "Dietetic"; with the addition of "Neonatal Diarrhoea", his scheme will be followed here.

My contribution to this discussion on ætiology will be to try to derive some estimate of the relative frequency of deaths from neonatal, infectious and parenteral causes, as they are happening in London at the present time. Much of the material needed for this analysis was obtained through the kindness of Dr. G. F. Buchan, the Medical Officer of Health for Willesden. The data consisted of the borough records of the deaths of infants under 2 years which were registered as "Gastro-enteritis", "Diarrhoea and Vomiting", &c., all diagnoses ultimately included by the Registrar-General under "Diarrhoea and Enteritis". Comparisons

prevalent in the locality at the time. Such a conception of the ætiology of enteritis thus involves the conjunction of several contingencies: first, contact with a potentially pathogenic strain; secondly, the absence of any specific congenital immunity against that strain; and thirdly, the loss of aciduric flora that follows the cessation of breast feeding. This seems to accord better with our knowledge of enteritis than the conception of a single bacterial malefactor that is capable of causing enteritis in all infants infected, which has tended to dominate bacteriological investigations upon infantile enteritis in the past.

In conclusion, for the purpose of focusing discussion, I shall summarize very briefly these views on the relative importance of these various forms of infantile enteritis in London. It seems to me that, in spite of the rise in the incidence of deaths from this condition in the late winter months, there is little evidence that parenteral infections play any important part in their ætiology. On the other hand, there seems to be evidence that the neonatal form of enteritis is rising and, with the increasing use of maternity hospitals, this rise is likely to continue. But the main component of infantile enteritis in urban communities seems to be Smellie's "Infectious" form. In the past, the infective agents were spread by two main vectors—flies and man—the one seasonal and the other perennial. The former has largely disappeared, and with it has gone the devastating outbreaks during hot summers. The latter continues and maintains the endemicity of mildly pathogenic organisms that are capable of causing enteritis in susceptible infants.

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In surveying results of the bacteriological findings from the fæces he noted that no specific organism had been isolated which could be accepted as the specific cause of the disease such as *B. typhosum* is in typhoid fever. Investigations had incriminated a long list of organisms, usually non-lactose fermenting Gram-negative bacilli such as *B. proteus*, Morgan's No. 1 bacillus, paracolon bacilli, sometimes dysentery bacilli, &c. He presented a selection of bacteriological findings from various investigators in different parts of the world during the last forty years. These included the findings of *B. proteus* in 93% of cases by Metchnikoff in Paris in 1914, the isolation of dysentery bacilli in 75% of cases by Biocca and Cammerella in Italy in 1939, the isolation of *B. morgani* by Morgan and Ledingham in London in 1904, the 50% frequency of paracolon bacilli reported in 1929 by Fothergill in the U.S.A., also found by Morgan and Ledingham. He outlined the results of his own work in Dublin which included a 50% incidence of *B. proteus*, 4% dysentery bacilli, 6.5% *B. morgani* and 30% to 40% of paracolon bacilli. He found that the majority of the latter organisms could be classified serologically, that four main antigens existed and that these paracolon bacilli usually contained common agglutinins with many dysentery bacilli. Correlation of bacteriological findings with the clinical course of the disease in Dublin showed that the isolation of *B. proteus* was statistically related to the severity and fatality of the disease process.

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problem—that of trying to make some estimate of the relative importance of the various forms of enteritis as they are occurring at the present time amongst infants in large urban communities. The circumstances which surround young children living a herd life in an institution are wholly different from those of the great majority of infants who live dispersed in ordinary houses and in contact with persons of all ages. The importance of infection in institutions is fully established: its importance in family life is not nearly so apparent.

The records for Willesden—a representative London suburban borough, both socially and epidemiologically—show that many of the deaths of infants from enteritis before the war were not distributed wholly randomly either in time or place, and less complete records from several other London boroughs have been found to support this conclusion. At the same time, little evidence was found in the Willesden survey of any outbreak in private houses which could properly be termed an epidemic. The outbreak which most nearly resembled one took place in the adjacent Wards 6 and 7 of the borough in the summer of 1935, when eight fatal cases occurred in a little more than three months within an area of less than a quarter of a square mile. Since the case-fatality rate for infantile enteritis about that time was of the order of 20% such a local outbreak probably led to clinical attacks in about 40 of the roughly 250 infants less than a year old who were living in the area. Although frank epidemics on their former scale no longer occur in London, and even small-sized outbreaks of the kind just mentioned are probably infrequent, there seems to be evidence in favour of the view that an infective factor is often in operation in the enteritis that is endemic in such urban communities. The instances of multiple fatal cases, such as were found in near-by houses and short roads in Willesden, as well as the raised incidence amongst twins, all acquire a certain cumulative force when taken together. It seems unlikely that so many deaths would occur in close proximity to one another unless they were connected either directly or through the intermediary of some surviving case.

Any discussion on the nature and mode of spread of an organism which might be responsible for such an infectious form of enteritis can at present be little more than speculative. The wide area of Willesden, over which more or less simultaneous fatal cases of enteritis were distributed, would suggest that any causative organism must at the same time be widely diffused, yet generally unobtrusive, in its behaviour in the general population. In comparison with what is known of the spread of nasopharyngeal bacteria in a community, little is yet known of the rapidity with which intestinal organisms, of species which are relatively harmless for adults and older children, circulate from person to person. What little evidence there is, however, seems to indicate that such exchanges are by no means infrequent. Wallick and Stuart made some observations on the persistence of particular serological strains of *B. coli* in the intestines of a subject by frequent sampling of his faecal flora. Their first identifiable strain was isolated in April, and it continued to be the predominant strain until the following September, when it was supplanted by the second. This persisted until the end of the year, when it was replaced by the third. If these observations are typical, and they are supported by other evidence of the same kind, it seems likely that the coliform flora of the human intestine undergoes frequent changes in its serological variants. It seems not improbable, therefore, that a coliform organism of a variety which is potentially pathogenic for certain infants may become disseminated freely in a restricted neighbourhood of an urban community—which shares many possible vector objects in common—without its evoking any noteworthy symptomatic reactions in the older population.

This conception of a low-grade pathogenic organism as the cause of infantile enteritis carries us back to the very carefully conducted field study of this condition that was made over thirty years ago by Peters in Mansfield. By selecting parts of the town for intensive study, he was able to obtain records over a period of about a year of the cases of diarrhoea that occurred at various ages of the population. The high rates in infancy and the more moderate rates in parents contrast with the much lower incidence in adolescents; deaths, however, were almost confined to the infants under 2 years of age. That the diarrhoeal attacks were of an infectious nature is supported by the great frequency with which multiple cases developed in the families attacked. Peters' findings are thus fully compatible with the view that strains of intestinal bacteria possessing very different pathogenic potentialities for infants and older persons are endemic in the population.

That *B. coli* itself can be highly pathogenic for newly-born infants is clearly shown by the occasional occurrence of a specific suppurative meningitis. So far as is yet known, the strain of *B. coli* which is responsible for this particular clinical manifestation is in no way distinctive, though serological studies on the lines initiated by Kaufmann in Copenhagen might lead to the identification of some particular variant of this organism analogous to that found by Pitman for *H. influenza*. Through the cessation of breast feeding and the resulting disappearance of the aciduric flora from the intestines, to which Cruickshank and others have drawn attention, the infant may become prematurely vulnerable to infection with any of the more pathogenic strains of coliform organisms that may happen to be

prevalent in the locality at the time. Such a conception of the ætiology of enteritis thus involves the conjunction of several contingencies: first, contact with a potentially pathogenic strain; secondly, the absence of any specific congenital immunity against that strain; and thirdly, the loss of aciduric flora that follows the cessation of breast feeding. This seems to accord better with our knowledge of enteritis than the conception of a single bacterial malefactor that is capable of causing enteritis in all infants infected, which has tended to dominate bacteriological investigations upon infantile enteritis in the past.

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were obtained in Birmingham, Alabama, by Davison in 1919 and by Denison and De Holl in 1935. In London in 1910, O'Brien could only find *B. morganii* in 14% of cases, although Morgan and Ledingham found this organism in 50% of cases ten years previously. He argued that we are faced with the alternatives that the pathogen is a different agent from time to time and from place to place or that the disease is of uniform aetiology and is due to a primary agent or cause, the nature of which is unknown.

Dr. Sevitt next described and criticized the evidence of viral aetiology. The work of Light and Hodes in the U.S.A., who claimed to have transmitted enteritis to calves with a filtrable agent from the stools, was suspect because the agent withstood boiling. Moreover Deeney in Dublin could not get these results with similar experiments. Reimann's experiments in transmission of diarrhoea to human volunteers by the inhalation of nebulized filtrates of gargle washings and stools were criticized on his failure to isolate the subjects from the rest of the community and the prolonged incubation period of one to three weeks in half his cases. The results of Christen and Buering-Sorensen in 1946 in finding a meningo-encephalitis or aseptic meningitis in many infants at post-mortem were not accepted as proof of viral aetiology as inclusion bodies were not demonstrated. Similar changes in the brain could be of toxic or nutritional origin. The speaker added that this might still be a profitable field of investigation.

In introducing a dual concept of aetiology he advanced epidemiological, histopathological and experimental evidence. The close association of incidence and fatality of the disease with the babies of the poorer sections of the urban population, the immunity of the infants of the well-off classes, the high incidence of the disease in many good working-class suburbs (where over-crowding was *not* a factor) and the relative immunity of the breast-fed infants of even the poorer classes all suggested some underlying nutritional factor or factors. Does breast-milk contain an anti-diarrhoeal factor? The close resemblance of the liver changes in diarrhoea with those found early in the course of tropical nutritional deficiency was in support of this thesis.

Next he outlined his experimental work with young kittens. He described the reproduction of a disease in 6 out of 13 kittens, which was clinically and pathologically similar to infantile enteritis, by the oral administration of serologically labelled type A paracolon bacilli. Noting that the resistant animals were usually heavier than the susceptibles he performed another experiment on 24 kittens, to test the combined and separate effects of malnutrition and infection. 12 animals were deliberately under-fed and 12 were well-fed. Half the animals from each group were orally infected with paracolon bacilli type A, the remainder were uninfected. The well-fed, uninfected animals all remained well; five of the under-fed, infected animals contracted diarrhoea, three of whom died; only two of the well-fed infected group had diarrhoea (one death) and only one kitten from the under-fed non-infected group developed diarrhoea which was not fatal.

Dr. Sevitt pointed out the fallacy of drawing unwarranted conclusions from animal experiments on a small scale, but, nevertheless, the results did suggest that the previous nutritional state is important in determining how many among the infected will contract enteritis, and how many will escape. Arguing further, and possibly incorrectly, to man there is support for a dual conception of the aetiology of infantile diarrhoea, viz. malnutrition and infection, the former acting as the underlying and predisposing cause, the latter as the exciting agent. While he recognized that neonatal outbreaks in nurseries and maternity homes were apparent exceptions to this theory it was worth further investigation.

Section of Endocrinology

President—L. R. BROSTER, O.B.E., M.Ch.

[November 26, 1947]

DISCUSSION ON SIMMONDS'S DISEASE. [Summary]

Professor H. L. Sheehan: NUTRITIONAL STATE IN SIMMONDS'S DISEASE.

The term "Simmonds's disease" will be used here to mean the clinical syndrome which results from a *long-standing and very severe* destructive lesion of the anterior pituitary. Such a lesion of the pituitary will be taken as the one essential feature of the disease, and the syndrome shown by patients with this lesion will be accepted as the true clinical syndrome of Simmonds's disease. The clinical diagnosis of Simmonds's disease in living patients should be based on this actual syndrome and on the specific evidence of the existence of the pathological lesion which can usually be obtained.

This interpretation is basically different from the two other common concepts of the disease:

(1) The usual definition of Simmonds's disease nowadays is that it is a syndrome identified by four cardinal characteristics: loss of weight, loss of sexual function, asthenia, low basal metabolic rate. This syndrome is usually accepted as clinical evidence of severe pituitary deficiency. In actual fact, however, as will be shown, most of the patients who have pathological proof of severe pituitary damage of long duration do not show all four characteristics of the syndrome; in particular, they rarely have a severe loss of weight. This definition is thus unsatisfactory.

(2) Certain authors maintain that the term "Simmonds's disease" should be confined to the syndrome, with its pathological basis, described by Simmonds in his original paper "On Disappearance of the Pituitary with Fatal Termination". Admirable though that paper is, it does not, however, give a perfect picture of what is now known about severe chronic hypopituitarism. Nevertheless it is of interest to note that Simmonds's patient (who was of medium height according to Leschke) had the quite passable weight of 103 lb. nine years after the onset of the disease. She died two years later. Simmonds mentioned that she was very thinned a few days before death, but he did not refer to loss of weight again.

In order to ascertain what is the actual syndrome which results from severe pituitary destruction of long standing, a detailed study has been made of the 103 published cases where post-mortem examination proved the existence of lesions of this type, whatever their aetiology. These can be accepted pathologically as incontrovertible cases of Simmonds's disease, and their clinical condition should therefore give a really reliable picture of the syndrome as it does, in fact, occur.

The state of nutrition of these patients *at the time of death* was as follows:

Fat	Good	Normal	Fair	Thin	Emaciated
9	11	36	19	14	14

These data are, however, of limited value. Simmonds's disease has commonly a duration of ten to thirty years. From the clinical aspect it is clearly more important to know the state of nutrition of the patients throughout the course of the disease than that of the corpses at the end of the terminal stage. (Some of the patients had died of wasting diseases such as tuberculosis, carcinoma, vomiting, &c.) For this reason a further assessment has been made of the nutritional state of the patients *at six months before death*. This appears to give a fairly representative picture of the nutrition throughout the prolonged course of the disease:

Fat	Good	Normal	Fair	Thin	Emaciated
9	11	57	11	9	6

These figures are obviously very different from the data of Escamilla and Lissner in

their Series A of "typical clinical cases of Simmonds's disease with pathological verification". The explanation lies in the different definition of Simmonds's disease; these authors adopt the second definition given at the beginning of this paper. A study of their 101 cases shows that 41 are acceptable as severe pituitary lesions of long duration; the remaining 60 cases showed lesions which were of only moderate or minor severity, so that they cannot be accepted as having produced significant hypopituitarism, or of such short duration that they cannot be accepted as having produced chronic hypopituitarism.

It is of interest to compare the present figures with those of 55 published reports of living patients with clinical evidence of very severe hypopituitarism of several years' duration following post-partum necrosis of the anterior pituitary. These patients had typical obstetric and clinical histories though, of course, there was no pathological verification of the lesions. Their state of nutrition was as follows:

Fat	Good	Normal	Fair	Thin	Emaciated
2	6	27	13	4	3

The present analysis has been restricted to severe lesions. From the study of 100 published cases of lesser degrees of pituitary damage proved by post-mortem examination, it appears that, if the remaining parenchyma is about one-quarter or one-third of the original gland, there is little or no pathological or clinical evidence of hypofunction. The survival of even one-eighth of the gland is often sufficient to prevent significant effects. The nutritional state of patients with lesser degrees of pituitary damage will not be discussed here except to note that the most emaciated patients usually have the most normal pituitaries.

All types of pathological lesions in the pituitary can produce various amounts of destruction of the gland. It should, however, be emphasized that pathological studies of the early and healed stages of post-partum necrosis show that this lesion is particularly liable to give rise to a very severe destruction of the gland. The clinical syndrome which results from this particular lesion is quite as complete as that caused by severe pituitary destruction from other causes. The fact that patients with this lesion are usually of normal nutrition must not be misinterpreted as an indication that they have a lesser degree of hypopituitarism; it is merely an indication that one of the hitherto-accepted standard clinical criteria of Simmonds's disease is not in accordance with the facts.

Dr. A. W. Spence: *Terminology.*

Simmonds's disease is variously referred to as Simmonds's cachexia, pituitary emaciation and panhypopituitarism, but the term is also used to describe lesser forms of hypopituitarism brought about by post-partum necrosis of the anterior pituitary, in which wasting is absent and only part of the endocrine system is affected. Simmonds (1914, 1916, 1918) in his original descriptions drew attention to the great loss of weight which may be associated with atrophy of the anterior lobe and for this reason called the condition "hypophyseal cachexia". Sheehan (1939) has shown that Simmonds's disease most frequently arises after a post-partum necrosis which is usually the result of collapse at delivery, but that more commonly incomplete forms of the syndrome develop after this incident. As a result of his observations he considers that the prevailing view that the fundamental symptom of Simmonds's disease is emaciation is erroneous. In my opinion if it is correct to apply the term Simmonds's disease to the milder manifestations of anterior pituitary insufficiency, as appears to be the custom in some circles, it is equally correct to apply the term to mild hypopituitarism caused by a lesion such as a tumour, since this was included by Simmonds as one of the causes of his syndrome. This, it will be generally agreed, would lead to confusion. I am of the opinion that if the term Simmonds's disease is used at all it should be applied only to those cases exhibiting manifestations of

panhypopituitarism brought about by an organic lesion, and not to those milder cases in which, for instance, the only feature of pituitary insufficiency is a disturbance of gonadal function. When more is known about the pathology and manifestations of a disease process, it is not always entirely satisfactory to describe the disease by a man's name, because cases may be included which clinically bear not the slightest resemblance to the original description. I think, therefore, that it would be more satisfactory to refer to Simmonds's disease and to the incomplete forms of the syndrome in terms of their pathology—post-partum necrosis, tumour, syphilis, &c.

Cachexia.—It has been doubted whether loss of weight is really directly due to a pituitary lesion and it has been suggested that any loss which may occur can be explained by a reduced intake of food. Experimentally it has been shown that removal of the pituitary causes cachexia and decrease of food intake and that injections of anterior pituitary extract cause an increase of food intake and of body-weight in the hypophysectomized animals (Smith, 1930; Richter and Wislocki, 1930). Clinically, in anterior lobe insufficiency loss of weight may occasionally precede loss of appetite. It is possible that the anterior lobe produces a hormone (? growth hormone) which is concerned with the maintenance of nutrition.

It has to be explained why many patients with post-partum necrosis do not lose weight and why some actually gain. Firstly, the degree of pituitary damage may not be sufficient to affect nutrition. Secondly, Smith (1926) has shown that injury to the tuber cinereum in animals results in adiposity. Since post-partum necrosis may sometimes damage the intermediate and posterior lobes causing polyuria, it is conceivable that it may also damage the tuber cinereum. The resulting tendency to increase in weight would counterbalance or more than counterbalance the tendency to lose weight that arises through damage to the anterior lobe.

Diagnosis.

The commonest cause of Simmonds's disease (panhypopituitarism) and of the incomplete forms is a post-partum necrosis. Apart from this, the disease is extremely rare and hence its diagnosis in men and in women who have not had a complicated delivery should be made with caution. The condition is diagnosed more often than it exists and on the other hand milder forms are overlooked. Dr. Russell Fraser will discuss the insulin sensitivity test and 17-ketosteroid excretion.

Myxœdema.—The clinical features of a post-partum necrosis may be confused with myxœdema, but although the basal metabolic rate may be as low as -40% , the facial appearance is not so heavy, the malar flush is absent, the skin is not so coarse and myxœdematous changes are rarely present. Primary thyroid myxœdema will not respond to injections of thyrotrophic hormone, whereas in hypothyroidism due to pituitary insufficiency the thyroid will respond to stimulation with thyrotrophic hormone and the basal metabolism will consequently rise. In doubtful cases this test is a useful adjunct to the insulin tolerance test and the estimation of the 17-ketosteroid excretion.

Anæmia.—Cases have been reported in which anæmia has been the predominant feature, but other evidence of pituitary insufficiency is usually present.

Wasting diseases.—The emaciation of Simmonds's disease must be differentiated from other wasting diseases and this may be difficult sometimes. Here again I would point out that unless the condition occurs in a woman with a previous history of a complicated delivery, the probability is that it is not a case of Simmonds's disease, but rather one of the commoner wasting diseases. Even if there is such a past history, one should be very careful to exclude a condition such as malignant disease.

Anorexia nervosa.—The disease *par excellence* which is confused with Simmonds's disease is anorexia nervosa. Continental writers in particular appear not to recognize anorexia nervosa as a clinical entity, but consider it to be a manifestation of hypopituitarism. Many of the cases reported as Simmonds's disease are typical examples

of anorexia nervosa. Admittedly the two conditions sometimes may be almost indistinguishable; even loss of sexual hair may occur in anorexia nervosa, but far less frequently than in Simmonds's disease; more usually there is a downy hirsuties. Lethargy and somnolence characterize Simmonds's disease, whereas patients with anorexia nervosa usually exhibit a surprising activity, but sometimes they may be lethargic. Differentiation rests mainly on the discovery of an initial psychological factor which is always present in anorexia nervosa.

As an argument against the view that anorexia nervosa is primarily a disturbance of the anterior pituitary, we cannot produce the statement that there is no evidence in the history of these patients that they had sustained any pituitary damage, because the protagonists speak of "functional Simmonds's disease" and "functional hypopituitarism". What refutes their hypothesis is that these patients get well with correct psychological management and without the administration of a single endocrine preparation.

I think that the existence of "functional Simmonds's disease" or "functional hypopituitarism" is possible. Since some cases of infantilism are probably due to a constitutional functional insufficiency of the anterior lobe occurring some time before puberty, a similar disturbance is not impossible after puberty. I wish to stress, however, that such a diagnosis should never be made before a disease such as anorexia nervosa has been carefully eliminated.

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Dr. Russell Fraser: DIAGNOSIS.

The term "Simmonds's disease" should probably be used broadly for all syndromes having loss of sex function, muscular weakness and evidence of generalized atrophy, in association with a demonstrable pituitary lesion. This excludes pituitary hypogonadism, whether eunuchoidism or amenorrhœa without other defect, and pituitary dwarfism with no muscular weakness. It may be necessary to establish the clinical diagnosis by two or more metabolic tests which can demonstrate the relevant pituitary insufficiency. Preferably one should measure gonadotrophic and the other non-gonadotrophic anterior pituitary function.

The demonstration of non-gonadotrophic anterior pituitary insufficiency is achieved by the combined use of at least two of the following three types of indirect test:

(1) An intravenous insulin tolerance test. This test involves a stress (hypoglycæmia) antagonized by the anterior pituitary gland, and assesses its efficiency better than any other test of carbohydrate metabolism.

(2) A urinary steroid assay. This indicates the level of adrenal cortical activity: a determination of 17-ketosteroids is the simplest method but it is also affected by gonadal secretion in the male. Kepler's test of adrenal cortical function is probably not so sensitive or so specific in less severe cases of Simmonds's disease.

(3) A test of thyroid function. An estimation of basal metabolic rate, or of protein-bound plasma iodine is the best, but an E.C.G. or an estimation of serum cholesterol may suffice sometimes. The value of a test of thyroid activity can be enhanced by daily injections of thyrotrophic hormone, which cause a rapid improvement in thyroid function where the deficiency is not dependent on primary thyroid disease.

The diagnosis of Simmonds's disease can probably be confirmed when any pair, except (2) and (3), of the above three types of tests show typical abnormalities of pituitary insufficiency.

Susceptibility to hypoglycæmia and hypersensitivity to insulin are well recognized features of anterior pituitary deficiency, but the twelve-hour fasting blood-sugar level, or the glucose tolerance test, are insufficiently sensitive to recognize these abnormalities except in severe cases (Escamilla and Lissner, 1942). The combined insulin and glucose test of Himsworth is no more satisfactory in our experience, as might be expected, because impaired absorption of glucose is a characteristic of Simmonds's disease and it interferes with the usual interpretation of this test as a measure of insulin sensitivity.

An insulin-tolerance test was shown by Houssay and Magenta (1924) to give a characteristic response in hypophysectomized animals. This has been confirmed frequently by others and a standard procedure has been evolved for clinical use (Fraser *et al.*, 1941).

This intravenous insulin tolerance test has shown significant changes in a series of patients with relatively mild Simmonds's disease in whom a history of a pituitary lesion was probable because other characteristic metabolic changes were present, and there was a typical post-partum hæmorrhage and shock at the onset of the disease, or evidence of a pituitary tumour (Fraser *et al.*, 1941).

In such cases there is a normal rapid fall of blood-sugar to hypoglycæmic levels followed by an abnormally slow return to the fasting level. The blood-sugar curve, which is expressed as a percentage of the fasting level, reaches its trough (50% of fasting blood-sugar $\pm 10\%$) within half an hour, but does not return to within 10% of the fasting level in the next two hours. This is called *hypoglycæmia-unresponsiveness* and is the opposite of what occurs in the diabetic patient (fig. 1).

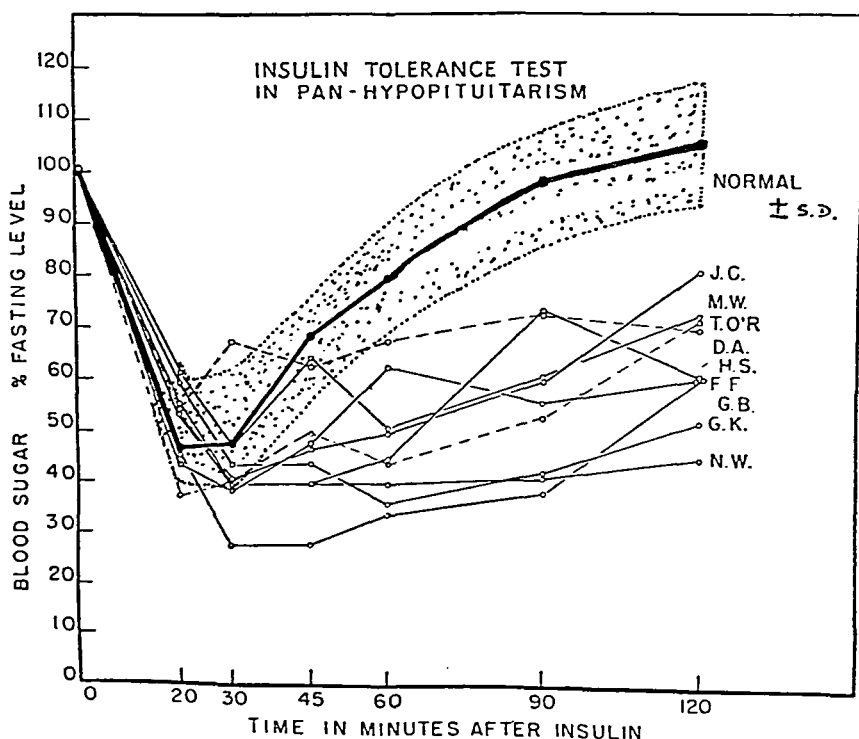


Fig. 1.—Insulin tolerance test curves from 10 patients with Simmonds's disease compared with the normal (see Fraser *et al.*, 1941, for case details).

The test is useful for distinguishing primary myxœdema, which gives a normal curve in mild cases, or an abnormally slow fall of blood sugar in severe ones; either result with a myxœdematous syndrome excludes anterior pituitary insufficiency. Patients with Addison's disease and hyperinsulinism show a similar abnormality to those with Simmonds's disease but they can generally be distinguished clinically. The test has been found to give a normal response in pituitary dwarfs without other evidence of pituitary insufficiency, in parapituitary diseases such as tumours compressing the hypothalamus without causing Simmonds's disease, and in uncomplicated primary or secondary gonadal defects. Severe hypoglycæmia should not occur with this test if certain precautions are observed (Fraser *et al.*, 1941). Any patients suspected of moderately severe pituitary deficiency should first be tested with one-third of the standard dose of insulin. If obvious mental confusion develops the test should be interrupted since this indicates abnormal hypoglycæmia-unresponsiveness. Meals should be given to all patients not less frequently than every three hours for the rest of the test-day. For approximately five days before the test patients should take a normal diet, including 250 to 350 grammes of carbohydrate per day. This is necessary for the correct interpretation of all carbohydrate tests. Severe general or liver diseases must also be excluded by clinical examination if abnormal hypoglycæmia-unresponsiveness is to be attributed to endocrine disease.

The urinary excretion of 17-ketosteroids is usually less than 2 mg. per twenty-four hours in Simmonds's disease (Fraser *et al.*, 1941), but a slightly higher level may be confirmatory in mild cases or when no correction has been made for non-specific colour formation. Similar very low levels of 17-ketosteroid output may also be encountered in severe liver disease, grossly defective intestinal absorption as in sprue, myxœdema and Addison's disease, and low levels, 2-5 mg. per twenty-four hours in women and 2-7 mg. in men, may be found in almost any case of general debility. The chief value of the test is to distinguish Simmonds's disease from anorexia nervosa and hyperinsulinism in both of which the response is usually about normal.

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Dr. S. Leonard Simpson: TREATMENT.

These observations are based on a study of six patients with unequivocal post-partum necrosis of the pituitary gland, observed during the past ten years.

Hypophysectomy leads to involution or atrophy of the thyroid, adrenal cortex and gonads, and deprives the body of other essential anterior pituitary hormones, especially the diabetogenic and nitrogen retaining factors. Patients with pituitary insufficiency, therefore, should be treated with thyroid, adrenal and gonadal hormones directly, or these should be replaced indirectly by the trophic hormones which stimulate the glands to renewed activity. In either case the substitution therapy must be continued unless spontaneous recovery occurs.

Thyroid.—Thyroid extract is needed in doses sufficient to raise a low B.M.R. and depress the blood cholesterol to normal. It must be given in gradually increasing doses, because it is as poorly tolerated as in myxœdema, and a patient may become much worse long before the basal metabolic rate approaches the normal (e.g. -18%), the symptoms being those of anorexia, nausea, vomiting, abdominal pains, collapse and shock. These symptoms have been interpreted as being due to acute adrenal insufficiency (Means, Hertz and Lerman, 1940; Lerman and Stebbins, 1942), and thyroid is better tolerated by patients receiving saline or desoxycortone.

The scalp hair is somewhat improved, but the pubic and axillary hair do not return. The final result of thyroid treatment is poor even when the B.M.R. is raised to normal.

Thyrotrophic hormone was used by Bulger and Barr (1936) in one case; the B.M.R. was raised from -28% to -3% , there was an increased rate of nitrogen loss and creatinuria, the patient lost weight and developed pyrexia, nausea and asthenia.

Adrenal cortex.—The Kepler test for adrenal insufficiency was positive in all the four patients in this series in whom it was tried. In one it was negative at first but it was repeated six months later and found to be positive. In the remaining two cases it was not done. The delay in water excretion was more marked than the changes in chloride and urea concentrations in the blood and urine. Subnormal values for blood chloride and sodium were present in the more severe cases although none showed elevated potassium concentrations. The 17-ketosteroid excretion was low in four cases (0.6, 1.5, 2.8 and 3.2 mg. per twenty-four hours) and normal in one undoubted one (12.0 mg. per twenty-four hours).

The assays were done by W. W. Payne and M. Reiss and N. H. Callow.

Desoxycortone.—In Case I the injection of 2.5 mg. of desoxycortone every other day produced some improvement in strength, appetite and well-being, but 2.5 mg. daily caused œdema of legs and 5 mg. daily severe water retention. In Case III there was a moderate clinical improvement when 5 mg. of desoxycortone was injected daily and subsequently this was maintained by the implantation of 400 mg. of desoxycortone. The blood-pressure remained low, and the patient very depressed, however, until methyl testosterone was given by mouth. In Case V the injection of 5 mg. desoxycortone daily produced moderate clinical improvement, but the blood-pressure remained at 90/60 mm.Hg and the patient was easily fatigued. When the dose was increased to 10 mg. daily the patient felt ill and developed œdema of face and lungs and dilatation of the heart. The blood-pressure rose to 124/70 mm.Hg, the serum potassium fell from 20 to 15 mg. per 100 c.c. and the serum sodium rose from 314 to 327 and chloride from 547 to 600 mg. per 100 c.c. In the three patients on whom it was tried desoxycortone proved of moderate clinical value only, and there was a considerable danger of overdosage.

Pig adrenal cortical extract, containing relatively large amounts of the carbohydrate-regulating factor, is likely to be of greater benefit than desoxycortone or salt.

Adrenocorticotrophic hormone.—Adrenocorticotrophic hormone was tried in two cases and apparently it was of moderate clinical value in one, causing an increase in the amount of pubic and axillary hair. The patient appeared to become refractory after a few weeks and local reactions were severe. Hemphill and Reiss (1944) reported good results in a woman aged 39 in whom the urinary excretion of 17-ketosteroids rose from 2.6 to 8.3 mg. per twenty-four hours.

Testosterone.—It is now well established that the adrenal cortex secretes androgens, and adrenosterone has been isolated from it. This is the explanation of the low output of 17-ketosteroids usually found in Addison's disease and Simmonds's disease, especially in women. Does an absence or diminution of androgens cause symptoms and signs in Simmonds's disease? The answer is a definite affirmative, both on experimental and therapeutic evidence. Hypophysectomy leads to a negative nitrogen balance which can be corrected by testosterone. In 1938 I demonstrated an anabolic effect of testosterone in hyperthyroidism, although the thyrotoxicosis persisted. Some months ago I showed at this Society two cases of surgical hypophysectomy, in which testosterone had abolished severe asthenia and produced an increase in weight and strength (Simpson, 1947). Jones *et al.* (1941) demonstrated that testosterone in eunuchoids produces an increase of B.M.R., a retention of nitrogen, sodium, potassium, phosphorus and water, and a fall in respiratory quotient. (? metabolism of fat). Weiner and West (1943) showed that methyl testosterone by mouth in hypopituitarism produces a retention of nitrogen, an increase in B.M.R., a return of the glucose tolerance curve to normal, a decrease in blood cholesterol, creatinuria and an increase in weight and strength.

In all cases in the present series, testosterone or methyl testosterone caused an increase in appetite, weight, strength, libido and eroticism, and a psychological improvement. It also produced a return of the hair in the pubic region, axillæ and eyebrows, and a darkening of the hair of the head. Initially 50 mg. of testosterone injected daily appeared to produce unfavourable results with nausea, malaise and mental disturbance. A total of 150 mg. of testosterone a week proved to be the optimum dose by injection; or 15 to 30 mg. of methyl testosterone daily by mouth. An implantation of 400 to 600 mg. of testosterone was also effective, but there was often a latent period of several weeks during which the patient was unwell. Implanted tablets of testosterone are sometimes extruded. It is interesting that testosterone abolished the hot flushes which occurred in two patients because they are usually ascribed to hyperpituitarism or more specifically hypergonadotrophic secretion (Albright, 1936) and Sharpey-Schafer (1940) found that testosterone may produce hot flushes in men with enlarged prostates or with eunuchoidism.

The hypochromic or hyperchromic anæmias sometimes associated with Simmonds's disease may not respond to iron or liver therapy unless testosterone is given also (Watkinson, McMenevig and Evans, 1947).

Progesterone.—Beall isolated progesterone from the adrenal cortex in 1938, and Emery and Greco (1940) found progesterone as effective as desoxycortone in prolonging life and maintaining growth in adrenalectomized female rats. It seemed likely, therefore, that it might be of value, perhaps more scientific than pragmatic, in Simmonds's disease. I was much interested to find in Case I that an implantation of 6 tablets of 50 mg. of progesterone, 5 of which were retained completely, produced a similar systemic effect to that of testosterone and caused growth of the hair on the pubic region, axillæ and eyebrows. Another patient, Case VI, has had a recovery of pubic and axillary hair-growth which had also failed to respond to œstrogen and thyroid therapy previously. Experimentally, progesterone has only a slight androgenic effect on mammals (Emmens and Parkes, 1939; Greene, Burrill and Thomson, 1940), but a definite effect on fishes (Eversol, 1941), and desoxycortone has a progesterone-like effect on monkeys (Zuckerman, 1940).

Estrogens.—Treatment with œstrogens causes some clinical improvement, but not as great as androgen therapy. The scalp hair increases in abundance, lustre and colour but the pubic and axillary hair do not recover, although in one case the eyebrow hair appeared to grow again.

Gonadotrophins.—Lerman and Stebbins (1942) found in one case of Simmonds's disease that 20 units of pregnant-mare's serum injected daily changed an inactive endometrium to a proliferative one, and produced libido, menstruation, better hair-growth on the scalp and eyebrows, and an increase in strength. Bécère and Simonnet (1946) found that patients with post-partum pituitary necrosis may have a failure of gonadotrophic secretion only with amenorrhœa, and they respond to a mixture of pituitary and chorionic gonadotrophins. The latter was tried in one patient only, Case I, and caused a dramatic allergic reaction which led to collapse and nearly proved fatal.

The treatment of hypoglycæmia.—Hypoglycæmia may be responsible for the peculiarities of behaviour and psychotic symptoms in Simmonds's disease, and it may cause death, as in one patient, Case II, who had repeated attacks of spontaneous hypoglycæmic coma. Lipoid extract of adrenal cortex (Upjohn), which is not yet available in quantity in this country, should be of value in this condition, although the injection of 15 c.c. in divided doses prior to the insulin-sensitivity test in one case did not restore the sensitivity to normal. It had a more marked effect, however, on the insulin-sensitivity curve in Addison's disease. It is probable that the pituitary diabetogenic and anti-insulin hormones are more important in preventing hypoglycæmia in Simmonds's disease.

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Dr. C. N. Armstrong mentioned a case of Simmonds's disease in a lady aged 49, diagnosed in 1936 by the late Sir Walter Langdon-Brown. Her illness had had an insidious onset over the previous two years and had not followed parturition. Radiological examination later showed the pituitary fossa was enlarged and there were calcified bodies in the enlarged pituitary gland. When seen by Dr. Armstrong in 1945 her health had deteriorated, and she had developed pulmonary complications. She was treated with corticotrophic hormone, and the following day her appetite returned. She continued to improve, her chest condition cleared up, and she began to put on weight. It was found that if corticotrophic hormone was discontinued for longer than two weeks she relapsed, and improved immediately treatment was resumed. The subsequent regime of treatment consisted of 10 units daily of Cortrophin (Organon), every alternate two weeks. On this routine her appetite was maintained, she enjoyed her food, and general improvement was upheld.

He mentioned another case which supported the remarks of previous speakers that oestrogens improved the condition of hair on the head in Simmonds's disease. A man whose hair had receded at the temples in a normal male manner developed feminism and subsequently his hair grew in a straight frontal line of feminine type. Thus it appears probable that oestrogens are responsible for the hair on the head and androgens for axillary and pubic hair.

[January 28, 1948]

Thyrotoxicosis in Mother with Cretinism in Child.—K. P. BALL, M.D., M.R.C.P., and BRENDA MORRISON, M.D.

Mrs. E. L., married woman, aged 32, had had a goitre for five years. She had never lived in an endemic goitre area and there was no family history of thyroid disorder. During her second pregnancy in 1946, she noticed increasing tiredness and sweating. Following childbirth, these symptoms became much more marked, her appetite increased, she lost weight and her goitre became larger.

June 1947: She attended the Central Middlesex County Hospital, where thyrotoxicosis was diagnosed. Basal metabolic rate + 47%. She was treated with methyl thiouracil, 600 mg. daily for three weeks, then 100 mg. daily with some improvement.

August 1947: She stopped treatment owing to headaches, and later she developed pneumonia and was treated at home.

December 1947: She was admitted to hospital with a relapse of thyrotoxicosis.

Basal metabolic rate + 60%. She was again treated with methyl thiouracil and has done well, gaining nearly one stone in weight.

Pamela L., born 29.1.47. Soon after her birth, her mother noticed that she would not take to the breast and failed to gain weight. She had a big tongue, a dry skin and an umbilical hernia. She was bottle fed after one month, but still would not take her feeds. At ten weeks she weighed 8 lb. 10 oz. Aged 3 months: Attended Great Ormond Street Hospital, where it was noted that she was a mouth breather, had a dry coarse skin and had a very large umbilical hernia. Blood cholesterol 162 mg. per 100 ml. Probable cretinism was diagnosed. She was treated with thyroid, gr. 1/8 b.d. and within a week she took her feeds normally and began to gain weight and became more lively. She continued to improve until aged 9 months. Treatment was stopped when mother became ill. At 11½ months she had no teeth, her anterior fontanelle was large and she had the appearance of a cretin. Blood cholesterol 298 mg. per 100 ml. She was treated with thyroid, gr. 1/4 daily, and has again improved.

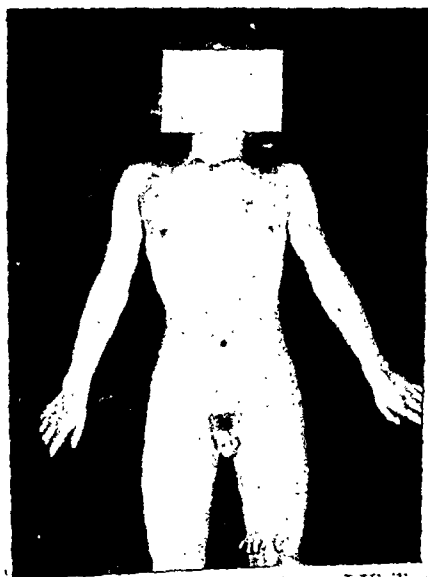
Adrenal Virilism (Group I). Bilateral Partial Adrenalectomy.—A. ELTON, F.R.C.S. (for L. R. BROSTER, O.B.E., M.Ch.).

Kay H., aged 9½ years.

September 1946: The case was sent up as a pseudohermaphrodite.

On examination.—Speech distinct, voice female; normal intelligence; legs boyish; markedly hypertrophied clitoris with urethra opening below this, enlarged prepuce, no scrotum, small vestibule, no vagina; pubic hair of female distribution (fig. 1). Marked muscular development. Blood-pressure 120/80. *Rectal examination:* small indefinite structure felt. ? infantile uterus and vagina. Urine—no abnormality.

X-rays: Epiphyses compatible with age 10 to 12 years; skull, no abnormality; adrenals, no calcification. Urinary 17-ketosteroids 44 mg. per day. Sugar tolerance curve normal. Diagnosis was then made of Group I adrenal virilism.



7.2.47: Laparotomy (L.R.B.). Both adrenals found to be four to five times normal size. Very small infantile uterus present. Both ovaries showed follicular cysts. A section was taken of each and showed normal ovarian tissue.

21.2.47: Right partial adrenalectomy, removing two-fifths of the adrenal; the part removed weighed 7 grammes.

4.3.47: 17-ketosteroids 12.1 mg. per day.

10.12.47: Seen again. Hypertrophied clitoris, some enlargement of breast tissue. 17-ketosteroids 26.2 mg. per day.

10.1.48: Left partial adrenalectomy. Left adrenal found to be five times the normal size and two-fifths of it were removed. Remains of right adrenal palpated and found intact.

Convalescence was uneventful. Present

17-ketosteroids 22 mg. per day.

Sub-total adrenalectomy for Group I Virilism.

Dr. Russell Fraser thought that bilateral partial adrenalectomy was particularly dangerous in this condition because of the reports of pseudohermaphrodites with adrenal cortical hyperplasia dying of Addison's disease.

Dr. A. C. Crooke said that a number of such cases had been reported now but adrenal cortical insufficiency with adrenal cortical hyperplasia and pseudohermaphroditism had so far only been described in infants and very young children and he thought that it was clear from the alternative that the only hope of relieving pseudohermaphroditism in patients like Mr. Elton's was bilateral adrenalectomy.

Section of Psychiatry

President—Professor Sir DAVID K. HENDERSON, M.D., F.R.C.P., F.R.S.E.

[January 13, 1948]

DISCUSSION: JUVENILE DELINQUENCY WITH SPECIAL REFERENCE TO REMAND HOMES

Professor Alexander Kennedy, (University of Durham):

Dis proximus ille
Quem ratio, non ira movet, qui facta rependens
Consilio punire potest.—Claudianus.

Few will deny that since the Children's Charter of 1908 the attitude of the Law and of public opinion towards the juvenile delinquent has become more liberal, humane and farsighted. Since that bloodless revolution in legal procedure the courts have by degrees transferred their interest from the nature of the offence to the nature of the offender and his circumstances. There has been since then an increasing recognition of the fact that in some cases punishment, so far from failing to deter the child from further antisocial behaviour, may sometimes even destroy his faith in society and foment his inward rebellion against its laws. The Act of 1908 gave expression for the first time in statutory terms to the view that the juvenile offender might be more sinned against than sinning and that the cause and the cure of his condition might emerge from an investigation of his background, which was and still is often one of poverty, of ignorance, of lack of outlet for normal energy or of disease and neglect.

In this important reform Psychiatry played no part, nor at that time had it much to contribute to the problem. The exposition of the psychopathology of juvenile delinquency in the novels of Dickens is far in advance of anything that psychiatrists could have written at the time. The position to-day is different and though great progress has yet to be made Psychological Medicine can contribute a great deal in certain types of case provided that the limitations of our present knowledge are fully realized.

The period between the Act of 1908 and the Children and Young Persons Act of 1933 was one of very uneven progress. In many areas there was little change in the attitude of magistrates, whose experience and interest were in any case with the adult offender and the Penal Code. Those who were interested in children, however, and in their social problems and in the prevention of adult crime began to realize the magnitude of their new responsibilities and the complexity and infinite variety of the factors of constitution and circumstance which were at work in the children who appeared before them only for a few brief minutes. They began to appreciate that each child presented a human problem the solution of which required infinite patience and kindness and no little specialized knowledge.

Some found it difficult to forsake the traditional impersonality of the Law and continued to make the punishment fit what they looked upon as the crime. They regarded with suspicion any tendency to lack of firmness in dealing with the young. Such an attitude is of course economical of time and of thought and it has its advocates even to-day. Only this year, however, has the Law removed from their hands the birch which reason and experience could not bring them to lay down. If he is to do justice to the children to whom he will be so important a memory, the juvenile court magistrate must go much further than mere interpretation of the Law and must now bring to his aid some of the method of science, the method of patient gathering of the facts, comparing them with previous facts, taking action only after careful consideration, observing the results and applying them to later cases.

It was logical that those who accepted these new responsibilities should invite scientific workers to assist the courts and the results of this co-operation were important. General recognition of the importance of mental defect and backwardness was perhaps the first important effect. The defective is not often punished for his stupidity nowadays but if we take a wide view of mental defect and do not confine it to intellectual defect as revealed by tests of intelligence we have still much to learn in this field. One of the after-effects of the outbreak of sleepy sickness in the '20s was to bring recognition of the influence of that disease on the power of ethical valuation in its victims and to draw attention to disease of the nervous system as a predisposing cause of antisocial behaviour. Here again the possibilities have by no means been fully explored. In the same way the application of the principles of psychopathology showed that disorders of behaviour could be the expression of emotional disturbance and that in some cases treatment based on this might have favourable results. This approach has fundamentally altered our attitude to the subject even though we now realize that full psychological treatment is indicated only in a minority of cases and that an excessive enthusiasm in this direction is not without its dangers. Lines of investigation such as these showed clearly enough that in many cases more detailed study of the children was necessary than could be done under existing arrangements, and the work of Clarke Hall, Burt and others pointed the way to the next step. The act of 1933 secured for the courts a framework of procedure within which they could, where necessary, find all the technical assistance they wanted. The court's decision was by now beginning to be more and more like a diagnosis, with a prescription for the treatment of the young offender.

Since 1933 there has been much trial and some error but in some areas great progress has been made. It is generally agreed that we have not yet got the best out of the Children and Young Persons Act, and in the matter of making the best use of specialized facilities for investigation, treatment and training there is still a long way to go. As more reforms come into effect, such as those contained in the Criminal Justice Bill, the need for a fuller understanding between the courts and their technical advisers becomes more urgent, and among those who assist the courts the psychiatrist occupies a unique position.

A psychiatrist is in a somewhat different position from the other specialists who assist the court in that he has been trained or should have been trained to make use of a team of investigators and to know enough of the work of each of them to assess its relevance to the case. He is better aware than the others of the possible pathological variations which may be found in the child and, as a rule, concentrates his own examination on the most difficult part of the investigation—on the child's attitude of mind and the mental dynamics of his behaviour. His more general review of the difficult case acts as a safeguard lest anything has been missed and in the statutory, medical and school reports there is no doubt that things frequently are missed. The psychiatrist's part therefore in ideal circumstances is to present to the court concisely and in plain language a living picture of the child's mental state with its potentialities and deficiencies, of the personal and social difficulties with which he is faced and of the probable reasons for his present conduct and attitude to life. He must also make definite suggestions for the child's future which are practicable in the light of existing facilities. The magistrate is then able to base his decision on a consideration of this report, upon his own observations and on the evidence.

In practice this system works fairly well in those courts where the magistrate and psychiatrist are both experienced and where they have worked together long enough to understand each other's limitations and where each realizes that every case is an experiment, the results of which must be carefully observed. A good deal of misunderstanding does arise, however, and the causes of this are worthy of review.

In the first place many magistrates who are baffled by a child's behaviour are apt to lean too heavily on the specialist and do not realize that he cannot be right every time. This may be the fault of the psychiatrist who is over-confident of his interpretation of the cases he sees but the inexperienced magistrate who finds him proven wrong by the child's appearance

in court again may lose faith in all psychiatrists and may tell his favourite psychiatrist story to all his friends. There are, of course, magistrate stories as well. If there are many inexperienced magistrates, the shortage of psychiatrists with sufficient training and experience to give the highest standard of service to the courts is even greater. Training in this branch of the subject has only very recently become part of the normal training of a psychiatric consultant. It is fair to say, too, that a psychiatrist cannot know enough about the background of juvenile delinquency until he has spent at least a year or so in examining cases and has had some contact with each of the many agencies concerned with the welfare of children; until he has done so his reports may reveal lack of knowledge of procedure, of the rules of evidence or of the facilities of disposal available for children. His theoretical training in psychiatry, too, needs very great modification when it is applied to this highly practical subject.

Magistrates are quite frequently irritated by the reports of psychiatrists in the early stages of their experience and there are some types of report which must be particularly irritating. Among these are the reports in which the psychiatrist recommends an entirely Utopian treatment, completely impracticable in the present state of organization of our children's services, or worse, implies that this treatment would cure the child but as it is not likely to be available, he washes his hands of the matter. Reports in which the psychiatrist defames the parents on the strength of hearsay evidence are, to say the least, embarrassing to the magistrate who wishes to read them out when the parents are present. Long-winded reports in which the magistrate seeks in vain for a clear-cut recommendation are of little practical value. Perhaps more serious are those in which the psychiatrist has paid scant attention to factors which the court realizes are important and has forced the case into a mould of psychopathological theory of one kind or another. Finally, magistrates may suspect, with reason in some cases, that technical verbiage may be hiding lack of experience or unwillingness to admit defeat. It is probably a sound principle both in Law and Psychiatry where there is so much technical language, that any view which cannot be put into plain English is quite likely not to be a sound one.

Perhaps the most important potential source of misunderstanding between magistrate and psychiatrist lies in the fundamentally different attitude of court and medical profession towards any defendant. A court is by constitution the protector of society whereas the doctor is by habit the protector of his patient and in the adult court he is frequently, perhaps too frequently, called upon to explain away his patient's behaviour. In the juvenile court his function is different; he is an impartial adviser, an excellent position for an expert witness which may, one day, be adopted in the adult courts. At the moment this position may call for some adaptation on the part of the psychiatrist if he is to strike a fair balance between his responsibility to society as well as to his patient. A similar effort of adaptation may be called for from the magistrate whose function in the juvenile courts includes that of protector of the child's interests.

The suggestion has often been made that the procedure of the juvenile court is too cumbersome and awe-inspiring to provide the sympathy necessary for dealing with children and that it might be replaced, as has been done in the Scandinavian countries, by a council of experts and social workers. In the United States, too, the juvenile court is a chancery and not a criminal court and it is my experience that technical evidence is accepted with far too little question in some American courts. In this country where the tradition of impartiality and fair trial is so strong I think we must regard with suspicion any tendency to substitute the technocracy of the child guidance clinic for the very democratic procedure of the courts. In particular I think we must preserve the principle that the individual may refuse investigations until it has been proved that an offence has been committed. The child should retain some rights as a citizen and contact with the dignity of the Law, suitably modified, is likely to do him no harm. It should be possible within our present system to arrive at a combination of British justice with an approach to the child which is both scientific and human.

The incidence of offences in general diminishes with age. It reaches a peak about the age of 13, when 13½ per 1,000 boys are found guilty in the course of a year, and falls rapidly as maturity is reached. Working with such material in which, in normal times, 70% of cases do not appear again after their first offence, in which over 70% of the lads sent to approved schools are not caught again within three years, it is easy to claim successful results for any method and apparent statistical success can be demonstrated for methods varying from the eye for an eye and tooth for a tooth theory to that curious religion to which some social workers appear to subscribe in which God is love and Sigmund Freud is his prophet, a faith which seems to have been a side-product of the development of psycho-analysis as we know it to-day. That such sophistries should be possible is a danger and one which can only be

averted by close follow-up of cases and by bringing home the results to those who have made the recommendations. The standard of not getting caught is hardly a test of citizenship and many of our apparent successes have merely learned to subvert the social order in some other way. The need for follow-up investigations on an entirely different scale to present methods is absolutely vital. No single factor can do more than careful follow-up to produce the humility in both magistrate and doctor with which both should approach their work.

Those who work with delinquent children are sometimes apt to think that the effect of the psychiatrist's examination is to make the case much more complicated and that probation officers or psychologists see the case in simpler terms. This would be an excellent reason for dispensing with the psychiatrist altogether were it not for the fact that human beings are very complex organisms and the more one learns to look for things in them the more one will find. This is particularly important in the case of children with constitutional abnormalities where early detection, while requiring the greatest experience and clinical acumen, is especially important owing to their potentiality for corrupting others. The children we see come for the most part from underprivileged homes but there are among them many whose handicap is neither material nor physical nor intellectual. It consists of a constitutional disability which comes gradually to light as their character develops and shows itself in an inability to march in step with their fellows, to form normal judgments and to feel a normal urge to conform to the rules of the community in which they live. In some cases this disability may be associated with abnormalities of the central nervous structure while in others these are not evident. As these individuals develop and fail to adapt themselves to living with other people the nature of the defect is revealed. Many of them merely suffer from their handicap but there are psychopathic personalities whose appearance in juvenile courts is the first sign of a condition from which society will be the major sufferer as they graduate from probation to approved school, from approved school to Borstal; from Borstal to prison and from prison to recidivism. Some of these can be helped if they are helped early enough, while for others society has not yet found a satisfactory remedy. That they should be recognized early and that their development should be under experienced observation and control is a necessity. At the moment cases of this kind reach the psychiatrist often only after they have upset the life of a remand home or an approved school, after they have stirred up trouble among their elders and in some cases after a variety of officials with strong views on treatment have accused each other of mishandling the case. More of these would undoubtedly be certified under the Mental Deficiency Act had not the assessment of mental deficiency so unfortunately become chained to the intelligence quotient in the minds of those whose duty it is to carry it out.

This group of rather depressing cases has been mentioned first in order to emphasize their importance at a time when the psychodynamic origin of behaviour disorder receives perhaps a disproportionate emphasis. It is fortunate that those in whom juvenile delinquency is a symptom of emotional disturbance are a larger group—children whose attitude and development have been stunted by emotional adversity and who need psychological protection, psychological first-aid or psychological treatment before they can stand alone among their more fortunate contemporaries. Many of these need protection only until the recuperative power of Nature, which is at least as evident in the field of mind as in physical medicine, has done its work. The dangers of over-treatment are considerable and it may often be enough simply to create the conditions necessary for natural recovery.

It has been suggested by experienced magistrates that every child who appears before the court should be the subject of a full investigation including a psychiatric examination. While no harm whatever can result from this in the hands of experienced workers the time and expense involved and the shortage of suitable qualified personnel make it almost impossible at the moment. The magistrates must thus be left to select those children in whose case they think investigation may lead to a better understanding and a practical improvement in disposal. We all know that cases of gross psychopathy, of nervous disease and of mental defect are sometimes referred for investigation only after their second or third appearance in court and the number of such cases to be found in approved schools bears witness to the frequency with which they are missed in court. When they are missed time is wasted and they are left free to corrupt other children in the streets. Dr. Scott has reported on an investigation which throws some light on the effectiveness of this selection in the hands of a group of experienced magistrates. As a result of this investigation it seems probable that their judgment should be assisted, except in trivial cases, by some sort of screening procedure. Such an examination, which could be made available both to cases remanded in custody and to children on bail or even on probation, might consist of a day spent at an observation centre during which group-tests could be given and play observed by experienced workers. If cases requiring further investigation were selected and added to those chosen by the court, it

might lead to earlier examination of those in need of specialized treatment and a greater possibility of rehabilitation before committal to an approved school becomes the only solution.

The selection of cases for detailed observation should, I think, be only one function of a centre of this kind. Some sort of clearing-house, in which information can be exchanged between those who are immediately concerned with a case, is badly needed—some means of ensuring continuity of investigation, treatment and subsequent follow-up. At present, if the court wish to carry out any special kind of investigation or if the case justifies a disposal or treatment which is out of the ordinary, considerable administrative difficulties may have to be overcome. In some areas the official machinery for dealing with delinquents has grown by accretion rather than by design and is cumbersome in operation. When the court has decided what is best for the child, the matter may pass into the hands of officials to whom the case is a paper transaction and whose interest in it is limited strictly to their hours of work and the failure of human material to fit itself into existing schemes for its disposal is a constant source of irritation to the less enlightened among them. It is a pity that the services of voluntary organizations have to be used so extensively to provide the individual attention and latitude which are needed in dealing with the young child and the first offender, and it is clear that in time all the facilities necessary for dealing with juvenile delinquents will have to be provided as part of the public service. The case for a central clearing-house combining the functions of observation centre, psychiatric clinic, social service exchange, record centre and treatment centre must be a strong one. In another place (*J. Ment. Sci.* 1948, In the press) I have set down the possible structure and functions of such centres which I believe should exist in a number of areas. They should be able to deal with cases in custody as well as with those coming up from their homes and treatment could be carried out on parents and children by the same unit who first found it to be necessary without the delay between diagnosis and treatment which at present so often reduces its value. Relatively few children need prolonged psychological treatment in my opinion but there are many who require a sort of psychological first-aid which must be given at the opportune moment. The opportunity afforded by the concentration of skilled personnel together with records and cases under treatment would provide an excellent background for the training of the many different types of specialist concerned with the young delinquent—among them the magistrate and the psychiatrist. In a number of parts of the world, centres of this kind already exist though in some cases their value is much reduced by a limited approach to the subject and adherence to one school of psychological thought. Enough has been learned from their efforts, however, for centres to be planned within the public service which would include their best features.

Our concern at the moment is almost solely with the child found to be delinquent. It is important that we remember that the offender who has not been caught is an even greater challenge. Although we may succeed with any one child who is brought before the court we are still powerless to prevent his younger brother from appearing as soon as he is old enough. We are often unable to prevent the potentially healthy but underprivileged child from passing his most impressionable years in a medium in which indifferent heredities breed in squalor and without healthy ideals of citizenship. A child's appearance in court is often only the presenting symptom of a malady, a defect of social adaptation which is afflicting his whole family or neighbourhood. A preventive outlook must be maintained even though the means at present at our disposal are greatly in need of further development. Nor would such an attitude be very new in relation to rebellion against the social order.

Χρή δὲ τοὺς ἐλευθέρους οὐκ ἀφισταμένους σφόδρα
κολάζειν ἀλλὰ πρὶν ἀποστήναι σφόδρα φυλάσσειν καὶ
προκαταλαμβάνειν ὅπως μὴδ' ἐς ἐπίνουαν τούτου ἴωσι.
(THUCYDIDES III, XLVI.)

Dr. P. D. Scott: The average annual number of cases brought before the London Juvenile Courts for the years 1940 to 1946 was 5,200, while the highest number remanded in any one of these years for the purpose of obtaining a psychiatrist's report was 630. The proportion of cases examined by the psychiatrist is thus a very small one and it may be of interest to investigate the criteria by which this proportion is chosen.

It is apparent that there are varying opinions as to the necessity for the psychiatrist's so-called "special report".

Vick and Curtis write "we gather that psychological reports are asked for rather freely—we are not altogether satisfied that they are not asked for too freely". Elkin on the

other hand writes: "It is impossible to visit many courts without becoming acutely conscious how great is the need for a wide extension of the facilities for medical and psychological examination." Cyril Burt was in favour of the examination of all but the trivial cases, remarking that otherwise the most hopeful cases may be passed by. He showed that 62% of cases where his recommendations were carried out appeared to be cured as compared to 12% where his recommendations were not carried out.

Hamblin Smith, referring to young offenders, said, "Every case requires individual investigation and consideration", and John Watson, "The ideal arrangement would of course be for the court to receive a medical report upon every child; . . . it is quite wrong that a bench of laymen should be charged, as at present, with the responsibility of making a 'spot' diagnosis of the cases which should be referred to the psychiatrist".

The consensus of opinion would therefore seem to be that ideally all but the trivial cases should be examined psychologically but that this at present is impossible. Reforms such as the setting up of remand centres may enable a greater proportion to be examined but even so the practical criteria for selecting cases for "special" reports will still be a problem.

Concerning this selection, Clarke Hall wrote: "No one without medical knowledge and experience can in all cases diagnose the necessity for a special report. Many children who may seem to a magistrate quite normal are in reality in very urgent need of such an investigation. . . ."

According to Elkin "it is only when a child is clearly unstable or presents obvious problems of behaviour that a request is made for a psychologist's report. But the effects of emotional stresses and conflicts are not necessarily obvious at first sight".

John Watson gives his opinion that, until better arrangements can be made, all cases of certain types should be referred as a matter of course—offences of a sexual nature, apparently motiveless offences and "peculiar" offences by which he is understood to mean those which one could not imagine an ordinary, mischievous child doing.

In an attempt to throw some light on this problem I examined 25 boys who had been sent to the remand home for purposes other than a special report, and compared them with 100 boys on whom I had been requested to make such a report. I shall refer to these as the non-referred group and the referred group. The selection was random except that in the non-referred group, cases upon which a previous psychiatric report had been made were rejected. Both groups were submitted to what I regard as the minimum adequate investigation. This consists of a physical examination, a psychometric examination, and at least two interviews with the child; the parents were requested to attend in every case and did so in 66% of cases and the reports of school officials, welfare and probation officers were studied. The object was to obtain as clear a picture as possible of the child and his setting, the family history, the development and present difficulties whether in the physical, social or emotional spheres, and to relate these difficulties (as well as the particular offence) to the total life of the child, thus determining their significance and appropriate treatment.

First as regards the charges: Table I shows a comparison of the charges in the referred and non-referred groups. The types of presenting symptoms which from the psychiatric point of view seem most strongly to indicate a need for full investigation are set out. These may be of practical use in a busy court-room. We may then compare these criteria with those evidently used by the magistrates.

(1) Stealing from the home is often found to be an act of aggression against the parents based upon unformulated feelings of deprivation and need for approval. The usual, and from our point of view most significant stealings, are those in which the child has taken the most cherished possession of a parent. I have for example four records in which the child stole his father's war medals, in other cases mother's clothing coupons, butter ration, and in one case a silver-framed photograph of a younger brother. It will be significant if the stolen goods have not been enjoyed at all but rather, as is usually the case, quickly thrown or given away or buried in the garden, or if they have been objects of which he could not possibly make any use. It is worth noting if the theft was precipitated by any particular incident and the emotional state of the child at the time. It is remarkable how little these emotionally determined delinquencies resemble the mischievous pranks of secure children. One boy of 10, less intelligent and successful than his sister, was given a lecture by his parents upon his poor school report. He went to his room and wept and then, when they had gone out, came down, stole the coal money, and dropped it down the drain in the road.

(2) Fire setting, wilful damage to property at home or elsewhere and what is referred to

in the courts as "grievous bodily harm" are overt aggressive acts which may be organically determined but more often have a similar motivation to the stealings already dealt with. They are mentioned here because it is felt that these highly antisocial acts and the intensity of aggressiveness displayed may arouse emotional reactions in those responsible for law and order thus possibly leading to summary punishment with forgetfulness of possible underlying psychopathology.

(3) Repeated lying, particularly of self-aggrandisement, or of accusations against the parents, usually indicates a need for investigation. One small boy who had been long evacuated returned to parents who no longer wanted him. He was physically well provided for and his management was outwardly correct but he persistently evoked the pity and pennies of strangers with stories of atrocities in his home, and reported himself at several police stations.

(4) Cases of wandering and persistently coming home late very commonly are due to remediable unhappiness of the child in the home and this is particularly likely to be the case if it is found that school conduct is relatively good.

(5) Persistent truancy is often associated with backwardness which leads to failure and discouragement at school and the natural wish to avoid such unpleasantness. Backward children are also likely to be less able to resist the lead of other boys in school who are truancy for other reasons and wish to bolster their courage by being accompanied. Psychometric examination may prove to be the most revealing part of their examination, but there are other truanters of good intelligence who show disturbances in other spheres dependent for example upon over-protection or, at the other end of the scale, neglect by their parents.

(6) Sex offences, though commonly discovered during the investigation are rare as presenting symptoms and always merit investigation. They seem to inspire a marked reaction particularly in parents and school teachers and are in no danger of being overlooked.

(7) Cases in which the disposal may possibly involve separation from home or change of foster home. Large among these will be the "Beyond control" and "in need of care or protection" cases which, I believe, should be referred unreservedly.

(8) Any repeated charge, or breach of probation would seem to merit investigation as indicating a failure of ordinary methods and a possible deeper significance.

(9) Young offenders should readily be referred for in them diagnosis is easier and the chances of successful treatment greater. The young child is also less likely to require remand in custody. The boy or girl of 16-17 may present a palimpsest of factors, many of them secondary effects of long delinquency. Unlike the younger children they may come to enjoy certain aspects of their delinquency and may have acquired a knowledge of the ropes and deeply ingrained attitudes and responses difficult to eradicate.

It will be noted that many of these indications fall within John Watson's groups—the sex cases, motiveless and "peculiar" offences.

Table I shows that all cases of stealing from parents, "grievous bodily harm", sex offences,

TABLE I.—REASONS FOR APPEARANCE IN COURT

Total number	Referred	Non-referred
	100 Actual no.	25 × by 4 for comparison
Breach of probation	7	12
Breaking and entering premises	8	8
Breaking and entering with stealing	18	24
Stealing (not from parents)	24	36
Stealing from parents	10	—
Grievous bodily harm	3	—
Sex offences	1	—
Wilful damage	1	4
Absconding from approved school	2	4
Truancy	10	—
In need of care or protection	3	—
Beyond control	13	12

truancy, "in need of care or protection" have been referred for examination, thus suggesting that the magistrate's criteria are largely the same as the psychiatrist's.

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It is clear to anyone who knows the difficulties which delinquent children offer, that it is impossible to recognize all the cases in need of special investigation and treatment unless all are examined fully as a routine. The following two cases are examples from the non-referred group.

CASE I.—A boy of 12 years, brought to court by his parents as beyond their control because he habitually stole from shops, truanted from school, stayed out late, was insolent and bad mannered.

A psychiatrist's report was not asked for. He was sent to the remand home pending the selection of a foster home.

Family history.—Father was a caretaker—steady man earning a regular wage. Mother was at home. She was an anxious, easily flustered woman, worn out by the constant moves from house to house which circumstances had imposed upon her. The boy was the youngest of five children each of whom had at one time or another presented a social or psychiatric problem. The home conditions and atmosphere were reported to be very bad.

Personal history.—As a little boy of 4 or 5, he had had *grand-mal* attacks, violent tempers, had broken windows in his rage and run his head against the wall. He was evacuated to the country, without his mother, and improved. At 8, he returned and his fits increased in frequency. He was admitted to a colony for epileptics, was reclaimed for a while by his mother but had to return. He was again taken out, against advice, and after several moves remained at home for a year before being brought to court. Major fits were occurring in groups at intervals of a few months. He was having no medicine. He had had no other illness or injury.

The school reported him as intelligent but intolerably insolent and unbearable in an ordinary school. On examination he showed no neurological signs and was well developed and well nourished. He had a habit spasm of his mouth and his nails were chewed down. He was shy, restless and tense, and it was difficult to gain his confidence. Even so his I.Q. (Binet) was 109. At a second interview he relaxed, and showed a photograph of his mother which he always carried round with him. "I would rather have 5 letters from her than 10 parcels" he said (children in the remand home are allowed parcels of fruit and sweets, but he had not received any), he told how he thought one of his sisters hated him and tormented him. Sometimes he felt an excited feeling inside him and then had to hold himself stiff, squeezing his arms against his sides. "When I leave you I shall have to go over everything I've said, I wish I could get out of it". He felt he had to touch certain things and count things on the table. In the Underground "something inside me says 'Jump on the line'". He indulged in many obsessional rituals.

The boarding-out officer was interviewed and found to be discouraged at having to find a foster home for this boy.

It was felt that he was at present incapable of settling either in his own or a foster home, that he needed treatment in a special residential school, and regular medication. His home offered a social problem upon which much work needed to be done if he was ever to return to it.

CASE II.—A boy aged 14½ had been brought to court three months previously as beyond the control of his mother. He had been placed under supervision of a probation officer who now brought him back because he refused to go to work. He had already been committed to an approved school when in the remand home. The father died when the boy was 5½. His mother was a hard-working, well-intentioned woman who had done her best for the boy. There was no history of nervous or mental disorder in the family. There was one other sibling, a boy, now settling well in the Army after presenting a very similar but less intense problem to this one. The mother said that he had been bottle fed, and had been cross and difficult as a baby. When he was between 2 and 5½ years she had been fully occupied looking after her husband in his long illness. The boy was a bed-wetter and got on his mother's nerves because he was "always wanting help with everything". He cried a lot when he had to go to school. At 6, he was evacuated, without his mother, for three years.

The real trouble started when he returned home. He was indolent and disinterested, took no notice of his mother, though he infuriated her with his careless ways and bed-wetting. At school he showed the same indolence and truanted regularly. Since leaving he had tried several jobs but showed no enthusiasm. He failed to attend the clubs to which the probation officer introduced him.

On examination he was in good health, quiet and apathetic, waiting until spoken to and answering with few words. His Binet I.Q. was 95. He did Raven's progressive matrices with some show of interest and scored 42 (Grade III). After several interviews a good rapport was obtained but he disclosed little useful information. He improved greatly during his time in the remand home: made good contacts with other boys, attended in the class room, read books with evident pleasure and could relate the story afterwards. He thus presented a picture of chronic apathy and depression, thought to be due to insufficient mothering as a baby, reinforced by long separation from home, loss of his father, and finally returning to an insecure home from which his mother was absent most of the day. It was felt that this chronically disturbed boy would be better away from home for a time, and that his outstanding need was the chance to make a firm emotional relationship with some understanding adult, in other terms, to gain a transference with someone who would know its significance and how

The remaining charges were evidently *not* considered indications for a special report and I would draw particular attention to the "breach of probation" and the "beyond control" cases.

Table II suggests in general that repetition of offence is not considered an indication for

TABLE II.—NUMBER OF APPEARANCES IN COURT

	Referred	Non-referred
Total number	100	25
	Actual no.	× by 4 for comparison
First appearance	41	40
Second appearance	21	36
Third appearance	18	8
More than third	20	16

investigation though there is a much smaller proportion of third appearances in the non-referred group.

Table III confirms that there is a considerable proportion of delinquents in both groups

TABLE III.—INTELLIGENCE

	Referred	Non-referred
Total number	100	25
	Actual no.	× by 4 for comparison
Above average	14	24
Average	36	44
Below average	34	28
Seriously dull	16	4

having intelligence above average and that the magistrates are able to recognize nearly all the seriously dull cases.

Table IV deals with causation. The classification with its four main headings, social

TABLE IV.—CAUSATION

	Referred	Non-referred
Total number	100	25
	Actual no.	× by 4 for comparison
Social factors	2	4
Personality	33	12
Mental conflict	5	12
Organic and psychotic	—	4
Combination of social and personality	44	44
Other complex combinations	16	24

forces, personality traits, "conflict" or neurotic delinquency, and the psychoses and organic conditions, has been adapted from a paper written by D. M. Levy (1932).

The psychiatrist (as opposed to the social worker) is mainly concerned with delinquency caused by personality traits and by "conflict" or neurotic mechanisms, and these factors, particularly in combination with other factors, are seen to be as well represented in the non-referred as in the referred group. As would be expected the cases showing combinations of factors appear to be the most difficult to recognize. The impression is gained (and particularly so in reading through the actual case-histories) that there was as great a need for psychiatric work in the one group as in the other. A similar impression has been gained in remand homes outside London.

The ages in the two groups have also been compared. In the non-referred group there is a peak age at 11 years while that of the referred group, as in most British studies in delinquency, is at 13 years. The percentage of children of 11 years and younger in the non-referred group was 28 while in the referred group it was 24 so that youthfulness is evidently not a usual indication for investigation.

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Family history.—Father was a caretaker—steady man earning a regular wage. Mother was at home. She was an anxious, easily flustered woman, worn out by the constant moves from house to house which circumstances had imposed upon her. The boy was the youngest of five children each of whom had at one time or another presented a social or psychiatric problem. The home conditions and atmosphere were reported to be very bad.

Personal history.—As a little boy of 4 or 5, he had had *grand-mal* attacks, violent tempers, had broken windows in his rage and run his head against the wall. He was evacuated to the country, without his mother, and improved. At 8, he returned and his fits increased in frequency. He was admitted to a colony for epileptics, was reclaimed for a while by his mother but had to return. He was again taken out, against advice, and after several moves remained at home for a year before being brought to court. Major fits were occurring in groups at intervals of a few months. He was having no medicine. He had had no other illness or injury.

The school reported him as intelligent but intolerably insolent and unbearable in an ordinary school. On examination he showed no neurological signs and was well developed and well nourished. He had a habit spasm of his mouth and his nails were chewed down. He was shy, restless and tense, and it was difficult to gain his confidence. Even so his I.Q. (Binet) was 109. At a second interview he relaxed, and showed a photograph of his mother which he always carried round with him. "I would rather have 5 letters from her than 10 parcels" he said (children in the remand home are allowed parcels of fruit and sweets, but he had not received any), he told how he thought one of his sisters hated him and tormented him. Sometimes he felt an excited feeling inside him and then had to hold himself stiff, squeezing his arms against his sides. "When I leave you I shall have to go over everything I've said, I wish I could get out of it". He felt he had to touch certain things and count things on the table. In the Underground "something inside me says 'Jump on the line'". He indulged in many obsessional rituals.

The boarding-out officer was interviewed and found to be discouraged at having to find a foster home for this boy.

It was felt that he was at present incapable of settling either in his own or a foster home, that he needed treatment in a special residential school, and regular medication. His home offered a social problem upon which much work needed to be done if he was ever to return to it.

CASE II.—A boy aged 14½ had been brought to court three months previously as beyond the control of his mother. He had been placed under supervision of a probation officer who now brought him back because he refused to go to work. He had already been committed to an approved school when in the remand home. The father died when the boy was 5½. His mother was a hard-working, well-intentioned woman who had done her best for the boy. There was no history of nervous or mental disorder in the family. There was one other sibling, a boy, now settling well in the Army after presenting a very similar but less intense problem to this one. The mother said that he had been bottle fed, and had been cross and difficult as a baby. When he was between 2 and 5½ years she had been fully occupied looking after her husband in his long illness. The boy was a bed-wetter and got on his mother's nerves because he was "always wanting help with everything". He cried a lot when he had to go to school. At 6, he was evacuated, without his mother, for three years.

The real trouble started when he returned home. He was indolent and disinterested, took no notice of his mother, though he infuriated her with his careless ways and bed-wetting. At school he showed the same indolence and truanted regularly. Since leaving he had tried several jobs but showed no enthusiasm. He failed to attend the clubs to which the probation officer introduced him.

On examination he was in good health, quiet and apathetic, waiting until spoken to and answering with few words. His Binet I.Q. was 95. He did Raven's progressive matrices with some show of interest and scored 42 (Grade III). After several interviews a good rapport was obtained but he disclosed little useful information. He improved greatly during his time in the remand home: made good contacts with other boys, attended in the class room, read books with evident pleasure and could relate the story afterwards. He thus presented a picture of chronic apathy and depression, thought to be due to insufficient mothering as a baby, reinforced by long separation from home, loss of his father, and finally returning to an insecure home from which his mother was absent most of the day. It was felt that this chronically disturbed boy would be better away from home for a time, and that his outstanding need was the chance to make a firm emotional relationship with some understanding adult, in other terms, to gain a transference with someone who would know its significance and how

The remaining charges were evidently *not* considered indications for a special report and I would draw particular attention to the "breach of probation" and the "beyond control" cases.

Table II suggests in general that repetition of offence is not considered an indication for

TABLE II.—NUMBER OF APPEARANCES IN COURT

	Referred	Non-referred
	Actual no.	× by 4 for comparison
Total number	100	25
First appearance	41	40
Second appearance	21	36
Third appearance	18	8
More than third	20	16

investigation though there is a much smaller proportion of third appearances in the non-referred group.

Table III confirms that there is a considerable proportion of delinquents in both groups

TABLE III.—INTELLIGENCE

	Referred	Non-referred
	Actual no.	× by 4 for comparison
Total number	100	25
Above average	14	24
Average	36	44
Below average	34	28
Seriously dull	16	4

having intelligence above average and that the magistrates are able to recognize nearly all the seriously dull cases.

Table IV deals with causation. The classification with its four main headings, social

TABLE IV.—CAUSATION

	Referred	Non-referred
	Actual no.	× by 4 for comparison
Total number	100	25
Social factors	2	4
Personality	33	12
Mental conflict	5	12
Organic and psychotic	—	4
Combination of social and personality	44	44
Other complex combinations	16	24

forces, personality traits, "conflict" or neurotic delinquency, and the psychoses and organic conditions, has been adapted from a paper written by D. M. Levy (1932).

The psychiatrist (as opposed to the social worker) is mainly concerned with delinquency caused by personality traits and by "conflict" or neurotic mechanisms, and these factors, particularly in combination with other factors, are seen to be as well represented in the non-referred as in the referred group. As would be expected the cases showing combinations of factors appear to be the most difficult to recognize. The impression is gained (and particularly so in reading through the actual case-histories) that there was as great a need for psychiatric work in the one group as in the other. A similar impression has been gained in remand homes outside London.

The ages in the two groups have also been compared. In the non-referred group there is a peak age at 11 years while that of the referred group, as in most British studies in delinquency, is at 13 years. The percentage of children of 11 years and younger in the non-referred group was 28 while in the referred group it was 24 so that youthfulness is evidently not a usual indication for investigation.

Mrs. Madeleine J. Robinson, J.P.: I will deal very briefly with three points as they affect the magistrates in the juvenile court: (1) Psychiatric examination and diagnosis. (2) Psychiatric treatment. (3) The need for follow-up and research.

(1) It always seems to me that the juvenile court acts as a sieve sorting out the more serious cases. Is our present mesh fine enough to ensure that cases needing psychiatric examination will be spotted at the earliest possible moment? Or should all cases found proved see a psychiatrist either (a) during remand in custody, or (b) during remand on bail. Many magistrates would welcome such a system but it is clearly useless to ask for routine psychiatric reports unless adequate trained staff is available.

Personal experience forces me to the conclusion that the facilities in the remand home for diagnosis have been very inadequate in comparison with those provided at a good clinic. This has been unfortunate as the more serious cases are generally remanded in custody. Sometimes the reports received have been little more than a rehash of the probation officer's report and until recently, in London, parents were not even seen. During the war and the post-war period cases were frequently remanded in custody because the waiting lists at voluntary clinics and hospitals were so long that it was virtually impossible to obtain reports quickly on bail. Such a situation is obviously undesirable as a fortnight's remand in custody is often unnecessary and may antagonize parents who would otherwise be co-operative. The services of a full psychiatric team with adequate time for their examinations are essential if the work is to be done properly at remand homes and it should surely be possible for such a team to deal with cases on bail and to carry out treatment where necessary.

(2) At present, when treatment is recommended while the child remains at home, the whole procedure has to be started *de novo* at a clinic or a hospital. The contact made between the child and the psychiatrist at the Remand Home is broken and there may be a long wait before new appointments can be made and treatment started.

Treatment may break down, either: (a) Because parents are too overburdened or too unco-operative to secure regular attendance or to carry out advice, or (b) because the gravity of the offences committed or the home conditions make it impossible to leave the child at home. In the first case many probation officers feel that a closer co-operation between the psychiatrist and the probation officer, either direct or through the psychiatric social worker, might sometimes prevent a breakdown. Where this cannot be prevented and in cases in which it is clear at the outset that the child cannot remain at home, the courts find themselves in a difficult position if continued treatment is advised. With the best will in the world it is often impossible to secure treatment once the child is removed from home. It therefore seems clear that treatment must be developed for children in institutions of various kinds.

(3) At present magistrates have very limited opportunities of learning from experience, because often it is merely by chance that they see the result of their decisions after a period of time and they have little or no basis of fact behind their theories. The London Juvenile Court Chairmen have pressed the Home Secretary to take powers in the new Criminal Justice Bill to initiate or aid research, including investigation into the results of treatment of various kinds. Such powers already exist in the new Health and Education Acts.

Mr. J. A. Rose, speaking as a magistrate who had experienced and appreciated the aid psychiatrists could and did render to the courts, said that not all magistrates were of the same mind. Many were sceptical and even regarded psychiatry as a fad. They had to be convinced of its value by argument, persuasion and, above all, by example. In the Provinces, where remand homes were often a long way away from the courts, liaison between the psychiatrist and the court had to be maintained by the probation officers. Though they were trained to value the aid of psychiatrists, they were rendered cynical, and therefore less co-operative, by recommendations which were completely impracticable.

The profession could greatly help to combat both the scepticism of magistrates and the cynicism of probation officers by taking trouble to ensure that their recommendations in particular cases were possible of application in the circumstances of the case, and were within the legal powers by which the action of the magistrates was limited. He quoted one example out of many which could be given, a case in which a psychiatrist recommended that a boy should be sent to a special school at a fee of ten guineas a week, when the total income of the family was round about six pounds a week.

He desired to see co-operation between magistrates and psychiatrists greatly extended and pleaded for assistance along the lines he had indicated.

to deal with it. Without this, the good qualities of an approved school would possibly be insufficient to ensure a permanent adaptation.

Where the psychiatrist has insufficient time to study his cases and to interview the parents, the magistrate will be justified in considering that as good a guess may be made in the court-room as elsewhere; also he may feel with a stubborn recurrent case, that the only disposal is an approved school and that once there it will not be of any advantage to the boy to have seen a psychiatrist. But the remand home psychiatrist should be able to help others than the magistrate—the parents to whom the child may return, the Home Office official whose task is to select a suitable school, the schoolmaster to whom he may be sent, the children's welfare officer who may have to select just the right foster-parent, and last but not least, he may be able directly to help the child itself. It is one of his tasks also to protect an approved school or other small community from the occasional case which is very disturbed, unreformable and likely to interfere with the welfare of the group as a whole. Such cases should be dealt with as maladjusted or epileptic or psychotic as the case may be. In the future the psychiatrist may be of use in selecting cases for, and in helping to run, therapeutic groups for delinquents or for parents of delinquents.

He should have sufficient knowledge of and interest in his cases to observe progress in the home or institution to which they will go and, if required, be prepared to give further advice and treatment. It is wrong that the remand home psychiatrist should not know the implications and results of his recommendations for only by follow-up studies is he likely to learn.

It behoves anyone who recommends an increased referring of children for psychiatric examinations, to consider any possible harmful effects entailed.

It will need additional staff. It will be costly, but prevention is likely to be cheaper than later maintenance of delinquent adults. For young and first offenders, and particularly if the remand is in custody, it will be at best a psychologically traumatic event which may increase feelings of resentment and thus foster anti-social tendencies. There is a certain stigma in the proceedings which may increase anxiety and feelings of inferiority in pre-disposed children. There is a risk of a child making bad associates, or being educated in delinquency and of a possible acceptance of his criminal destiny. One must consider also the feelings of the family and what will be the effects on the children in his street and school of his lurid story of "a cushy fortnight inside".

These are mostly problems of the remand home or centre and are arguments in favour of avoiding remand in custody rather than avoiding the actual examination. The latter also, however, may have its dangers.

The psychiatrist must guard against a sentimental attitude which may help the delinquent to rationalize his trouble as purely the fault of his parents or circumstances. Even where there is a demonstrable psychopathology in need of treatment, the salutary effect of appearing before the magistrate should not be depreciated by subsequent experience with the doctor.

It is possible also that a psychiatrist after a time may find problems where they are not, mistaking molehills for mountains. This will best be prevented by working also with non-delinquents, following up cases, and bearing in mind the normal surroundings and behaviour of the types of children with which he deals.

In conclusion, it seems desirable to examine the majority of cases and to avoid remand in custody whenever possible. Until this can be brought about the present methods of selection, as practised in the London Juvenile Courts, seem sound and effective though a proportion of cases needing special investigation and treatment escapes the mesh. When increased facilities will be available a start should be made by adding all youthful cases, all cases remanded in custody, and all cases charged with being "beyond control" or with breach of probation.

The remand home psychiatrist should be prepared and given the opportunity to extend his field of operation and thus justify the referring of cases to him for wider purposes than diagnosis and immediate disposal.

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Section of Medicine

President—MAURICE DAVIDSON, M.D., F.R.C.P.

[January 27, 1948]

DISCUSSION ON THE DIETETIC SERVICE OF THE HOSPITALS OF THE FUTURE

Lord Woolton, in opening the discussion, said that when he was Minister of Food he found that some people thought of food merely as a means of satisfying the pangs of hunger, while others more fortunately situated ate for pleasure. It was true, however, that few people chose meals for their actual food value. Neither were they guided by the natural instinct for selecting the right foods, as nowadays they had to take whatever was available in the largest quantities; this applied especially to manual outdoor workers.

In hospitals he had been appalled by the way the nurses' food was cooked and prepared; a start might be made by improving this side of hospital catering. There would be a tremendous influence on the health of the nation if every convalescent could be given elementary lessons in food values. Advice on food values should be obtainable in all medical institutions and at Infant Welfare Clinics; at the latter particular attention should be given to the feeding of expectant and nursing mothers.

Sir Jack Drummond: In considering what should be the future developments of this vitally important part of hospital services it is useful to have as a background impressions gained from a study of the past and of the present.

It is not surprising, when one bears in mind the evolution of our hospitals from the charitable institutions for the very poor, which they were until well into the nineteenth century, that many ideas, deeply rooted in tradition, survived so long.

The provision of food for patients in earlier times was very much a secondary consideration. One square meal a day, whether the diet was full or low, was thought to be adequate whilst parsimony in the kitchen was regarded as commendable. It is in this early history that we can clearly trace the origin of the one cooked meal a day, still a feature of not a few hospitals, of divided control, of the confused interrelation between nursing and catering and of the misdirected efforts towards cutting the cost of food so often made by hospital managements.

In 1942 I was privileged to be invited to become Chairman of a special Committee set up by King Edward's Hospital Fund to examine and report upon hospital diets.

Dr. J. D. W. Pearce: It is important to bear in mind, when assessing the adequacy of psychiatric reports, the facilities which the psychiatrist has for the investigation of his patients. There have been instances where the time available and the information furnished to the psychiatrist by other sources have been so meagre as seriously to cripple him in his work. Reports for courts should be short and very much to the point. Opinions should be expressed quite clearly and in simple language. It is irritating for a magistrate to find that the psychiatric report includes long excerpts from the probation officer's report. Professor Kennedy referred to the need to regard mental defect not simply as intellectual defect, but also as including temperament defect. My own experience has been that the largest single group of juvenile delinquents is that in which temperamental instability is the most prominent feature. Where this is really severe and amounts to psychopathic personality proper, the ordinary approved school does not seem to be the proper milieu for the case, and there is quite urgent need to make special provision for such cases, both male and female; special approved schools or colonies may be the solution.

In the Criminal Justice Bill of 1947 the provision of State Remand Homes has been omitted. In the 1938 version of the Criminal Justice Bill provision was made for such Homes, which would in point of fact be the observation centres, to the need for which Professor Kennedy has referred. Such State Remand Homes were also to have dealt with difficult cases in approved schools, such cases being sent to the State Remand Home for a period not exceeding three months. It is to be hoped that they will be reinstated in the new Bill.

The Institute for Scientific Treatment of Delinquency has, on behalf of the Home Office, been giving trainee probation officers comprehensive, good, general training in psychiatry. I myself have advised such trainees to contact their local psychiatric services in their own districts, and as these officers have some insight into psychiatric work, they are no doubt quite capable of assessing how good or how bad such local services are. Similarly elsewhere I have advised general practitioners faced with problems of delinquency to co-operate with the probation officer and to seek his help and advice where necessary.

Finally, surely the time has come to amend those laws which conflict so patently with the known laws of biology. Examples of these are the age limits at which a boy can have carnal knowledge, or a child have *mens rea*. In some cases the whole situation becomes absurd, e.g. where a boy under the age of 14, who on all the facts has committed a rape, cannot be charged with this as the law holds that until he reaches his fourteenth birthday he cannot have carnal knowledge.

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with the feeding of the patient. Miss Broatch has recently visited the U.S.A. to study their systems of hospital feeding. In many respects they are far ahead of us. Catering is almost everywhere unified and separated from nursing. Dietitians dominate the picture there, but those concerned with hospital administration are now admitting that they have gone a bit too far in handing over control to these experts. The personal touch between nurse and patient has suffered.

The members of the King's Fund Diet Committee feel that this important contact should be maintained. Every stage in the provision of food for the patients should be under the Catering Department until the meals reach the ward. Then, the nursing staff, who know the likes, dislikes and whims of the patient, should take over the actual service.

Dr. H. L. Marriott: Food in hospitals is a subject of immense importance in regard to the physical and psychological welfare of the patients. Their physical nutrition is a matter of significance in all but the most trivial medical and surgical conditions while in perhaps 30% of the total patients of an average general hospital suitable special dieting is the chief factor in treatment. One has only to think of such common conditions as diabetes, peptic ulcer, liver affections, sprue, prolonged fevers, conditions of protein depletion and conditions of fluid balance variations.

The psychological aspect of the feeding of hospital patients should need no emphasis. Anyone who has had an illness well knows that meals are most important events in his day-to-day life as a patient.

Unquestionably "the food service should be regarded as one of the essential remedial services offered by the hospitals" (King's Fund Report, 1943).

The aims of the food service should be to provide abundant food of first-class quality, well cooked and attractively served, with plenty of variety and choice. Furthermore, the food supplied to each patient should be nutritionally adequate and appropriate for his needs whether he belongs to the majority of patients who merely need good feeding or to the large minority needing special diets.

Our present hospital food services for patients and nurses do not fulfil these aims though, fortunately, the tendency is one of improvement. The lamentable facts of the matter were admirably demonstrated in the classic Memorandum on Hospital Diet published by King Edward's Fund in 1943.

The main cause of the low standard of past and present hospital feeding lies in the fact that hitherto the medical and nursing professions have failed to attach sufficient real importance to feeding, and many individual doctors and nurses have lacked accurate knowledge of nutritional facts. Our ignorance has been partly due to the relative newness of the science of nutrition but also largely to the fact that food is so familiar that we are apt to assume that we know all about it and have little to learn, whereas we treat with much more respect and humility subjects seemingly more recondite such, for example, as the rhesus factor or radiotherapy.

Perhaps the most basic elements of nutritional knowledge concern the simple facts of the daily dietary requirements of man (water, calories, protein, mineral salts and vitamins) and the knowledge needed to translate these requirements into terms of food—the food values of the common foods such as milk, meat, fish, eggs, bread, butter and sugar. Experience in consultations and in examining medical students and nurses suggests that these simple facts are not well known. Yet these same doctors, nurses and students are simply bursting with knowledge about details relating to matters infinitely less practically important and far harder to grasp.

The first memorandum¹ issued by this Committee presented many grave criticisms of current practice. Cases were described in which the nutritive quality of the diets was seriously defective: daily intakes of protein as low as 40 grammes; of vitamin C, 3 to 6 mg.; of vitamin A, none at all for six consecutive days and calorie intakes as low as or lower than the bare basal requirement. The standard of cooking and of the service of meals was reported as, in general, deplorably low, whilst inefficiency of administration and waste often went hand in hand with divided responsibility and control.

A strong case was made out for bringing all branches of hospital catering under the control of a single Catering Department, with a competent catering expert assisted by a dietitian in charge.

After the publication of this memorandum the Senior Dietitian of the King's Fund, Miss Broatch, visited a large number of hospitals and advised the Governing Bodies. This experience provided the material for a second memorandum, issued in 1945, which was essentially constructive in character². It provided suggestions for the unification of hospital catering under a single and expert control, for establishing Diet and Catering Committees in each hospital, for improving financial control, for staffing kitchens and also gave helpful ideas about planning menus and the service of meals.

It is encouraging to know that many hospitals followed this lead and that much progress towards more efficient catering has been recorded. On the other hand, reports by the Fund's dietitians still often make depressing reading; monotony of diet; the same menu repeated on the same day of each week; unattractive service; cold food; sodden and discoloured vegetables; only one cooked meal a day; no alternative to milk puddings, so the dreary records read. These are bad enough, but the shock is even greater when one discovers, by no means infrequently, that no related records are kept of the purchase and issue of food or that the full rations and allowances are not taken up.

It must be recognized that catering is to-day a very highly skilled job. Purchasing in the best markets, contracts, checks on purchases, stocks and issues, expert supervision of a kitchen, and control of waste are not matters that a matron or a house-keeping sister can fairly be expected to deal with nowadays in addition to her main duties. The catering of a hospital should be run as efficiently and as smoothly as that of a good hotel.

The science of nutrition has expanded so rapidly in the past twenty or thirty years that it needs the knowledge of a well-qualified dietitian properly to plan diets, not only in regard to their nutritive value but also their variety and appeal. Here, again, the field has grown too wide for those whose primary training is in nursing to have more than a superficial knowledge.

The planning of, and choice of equipment for, hospital kitchens call for much to be done in the future. Restrictions on building and on supplies of apparatus make improvements difficult to achieve at the present time, but there should be serious thought given to plans for the future. It is often said that the kitchens of many of the smaller hotels and restaurants would not bear inspection. I can assure you that that is certainly true of some hospital kitchens, and they have not even the saving merit of producing eatable meals.

In one connexion it appears desirable to retain the contact of the nursing staff

¹Memorandum on Hospital Diet. King Edward's Hospital Fund, London, July 1943.

²Second Memorandum on Hospital Diet. King Edward's Hospital Fund, London, May 1945.

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The main cause of the low standard of past and present hospital feeding lies in the fact that hitherto the medical and nursing professions have failed to attach sufficient real importance to feeding, and many individual doctors and nurses have lacked accurate knowledge of nutritional facts. Our ignorance has been partly due to the relative newness of the science of nutrition but also largely to the fact that food is so familiar that we are apt to assume that we know all about it and have little to learn, whereas we treat with much more respect and humility subjects seemingly more recondite such, for example, as the rhesus factor or radiotherapy.

Perhaps the most basic elements of nutritional knowledge concern the simple facts of the daily dietary requirements of man (water, calories, protein, mineral salts and vitamins) and the knowledge needed to translate these requirements into terms of food—the food values of the common foods such as milk, meat, fish, eggs, bread, butter and sugar. Experience in consultations and in examining medical students and nurses suggests that these simple facts are not well known. Yet these same doctors, nurses and students are simply bursting with knowledge about details relating to matters infinitely less practically important and far harder to grasp.

The first preliminary to getting our patients properly fed is that everyone in or connected with our professions must become imbued with the importance of feeding and primed with accurate nutritional knowledge. The onus for achieving this general attitude of mind lies particularly on those of us who are teachers of Medicine. Especially must we try also to convince our administrative boards of Governors and administrative officials that first-class food for the patients must be one of their chief aims, more important even than wonderful operating theatres, superb X-ray departments or magnificent board-rooms.

A corollary of the recognition of the necessity for better food services is that hospital managements must spend much more money on food and the food services. In the past hospital food has unfortunately been mainly scrutinized by hospital managers from the point of view of economy of expenditure. This emphatically must stop and their first preoccupation must become the quality of the remedial food services.

There should be a hospital Food Committee which should rank as one of the most important committees of the hospital with a forceful Chairman. The committee should meet not less than once a month and it should contain members of the hospital board, members of the medical staff, the superintendent, the caterer, the dietitian and the matron. The Food Committee should appoint from its members food inspectors who pay surprise visits, at least weekly, to wards, kitchens, &c., and who should concern themselves primarily with the quality of the food services and secondarily with matters of economy.

At the Middlesex Hospital we have had such a Food Committee for over two years and it has been very successful. Its success has largely been due to the voluntary work of its Chairman, Mr. W. B. Morison—a member of the lay board.

A catering officer should be responsible for all matters affecting food, including its buying, preparation and service, thus ensuring that a single individual is responsible for the hospital food. The catering officer should be the one person ultimately responsible, and should be regarded as subordinate only to the superintendent. The catering officer must be supported by provision for the food service of adequate personnel, accommodation and equipment—especially personnel; the service of food to the individual patient would seem best left a responsibility of the nursing staff, who have special knowledge of each patient.

Special diets should be the responsibility of the dietitian or of a special dietitian if the catering officer is a dietitian, and should be provided from a special diet kitchen or subdivision of the main kitchen. This special dietitian has in her hands the main form of treatment for perhaps one-third of the patients. If the catering officer is not a dietitian, then she will be the adviser on the more specialized aspects of hospital dietetics.

The dietitian must have adequate staff and facilities not only for routine day-to-day treatment but also to co-operate in research work requiring the provision of special diets. I would like to pay tribute to the great pioneer work done by the lady dietitians of this country and to draw the attention of the meeting to the great shortage of trained dietitians.

Captain H. Brierley: I am a hospital administrator who has spent many years managing the diet department. Hospital catering should be carried out by an expert caterer with some knowledge of dietetics who would be responsible for the whole diet department from the buying to the service of the food. In certain cases it

may be advisable for a hospital to appoint a dietitian to the post, but unfortunately few dietitians have sufficient good catering experience. I maintain, however, that good catering is the first essential and that a correct diet will follow. In large hospitals I think it is wise for the caterer to have a trained dietitian on his or her staff, and if this is a nurse dietitian, so much the better; she then acts as a very good liaison officer between the nursing staff and the caterer who should be directly responsible to the senior administrative officer. Any hospital feeding 200 patients plus staff should have a caterer and a dietitian and I am sure the money spent on salaries will not be wasted. The caterer must be allowed to have sufficient, well-paid, skilled staff to assist him and an up-to-date department with modern equipment. The department must have adequate offices so that there can be complete control of the ordering, checking, costing and stocktaking. There must be good central stores for all types of food where they may be properly stored and then prepared centrally by trained staff, as, for example, a butcher's shop where carcasses can be cut up and prepared, a fish shop where fish can be filleted, a butter room, a milk room, &c. There should also be a vegetable preparation room where all vegetables can be prepared for the kitchens centrally under supervision. The dry goods stores should be adequate and be provided with vermin-proof bins.

The dietetic service is divided into six main parts, the buying, storing, checking and costing, menu making, cooking and service. The menus should be the responsibility of the caterer, but they must be prepared in consultation with the dietitian and the chefs and they should be scrutinized and criticized from time to time by the senior executive officer. It is so very easy to get slack in drafting menus and in the past hospitals have been justifiably criticized for disgraceful planning of the food.

There should be adequate choice on the menus so that almost every diet can be catered for by the person who is ordering from the ward.

Cooking.—The number and general layout of kitchens is a most disputed subject. Some people advocate one large kitchen as being more economical and others believe that each ward or floor should have its own kitchen. I personally think that there is a happy medium, but certainly in a large hospital there should be more than one. I myself like one kitchen for patients, one for all staff and one for private wards. In addition it is wise to have a central pastry and sweet kitchen, under a skilled chef, which can serve everyone, as there is more satisfaction given and more economy carried out by a first-class pastry kitchen than in any other type of kitchen at the present time. I also advocate a central salad preparation room for everyone so that all salads and hors d'œuvres can be prepared under cool conditions and properly supervised away from the cooking.

I think a dietetic kitchen is desirable but this should be run as an annexe off one of the main kitchens so that reasonable economy can be exercised. It is absurd for a dietitian to be boiling a small saucepan of potatoes whilst exactly the same potatoes are being cooked next door. The dietitian should use the general facilities as far as possible. This special kitchen should be used for all highly specialized diets that need *separate* cooking, for all research diets and for training student dietitians. It should not be abused and one must therefore have a sensible dietitian in charge—not a crank.

So much for kitchens and cooking. The next essential is first-class delivery and this depends on the geography of the hospital. The food must be really hot when it leaves the kitchen and it must be conveyed in properly constructed and covered dishes in either electrically heated or insulated trolleys. The food must be delivered punctually and in the least possible time. This necessitates good administration.

The service of the food is a most important side. I think it should be under the supervision of the Sister and not the dietitian. The nurse knows much more about the patient and can see so much better to the helpless patient. It is so useless for a smart-looking dietetic student to take to a patient a beautiful tray and place it so that the patient cannot reach it, or possibly the patient may not be able to feed himself, and this is where the trained nurse should supervise. I think the dietitian should visit the wards regularly both at mealtimes and other times and advise on diets, also, should the hospital be training dietetic students, these students should spend part of each day working under the direction of the ward Sister.

The actual service can be done direct from the electric trolley going from bed to bed or the food can be served from a properly fitted ward servery. I myself think the latter is best and can be done more satisfactorily.

Every patient for every meal should have a tray, properly laid with good cutlery, salt and pepper pots and freshly filled clean glasses, taken in by a nurse or student dietitian one at a time. The plates should each have a cover which is removed by the nurse when she places the tray.

Hospitals should provide four attractive well-served meals in each day with plenty of variety for the patients and only one of them, namely tea, should be prepared in the wards.

Miss M. C. Broatch: *It is not sufficient for hospitals to appoint a catering officer and expect the feeding to improve immediately. The officer appointed must have the full backing of the Committee of Management; without this he will fail. The hospitals where this has happened must realize that it is those in authority who probably failed in their responsibility and not the Catering Officer. Sir Jack Drummond has referred to the service of meals to patients in America, where it has been entirely divorced from nursing. In the second Memorandum on Hospital Diet, it was recommended that the service of food was an important part of the nurses' duties. Nevertheless, this service is in danger of breaking down, unless steps are taken to see that due importance is given to the teaching of nutrition to nurses, not only in theory but in its application in the daily routine care of the patient.*

Miss D. F. Hollingsworth, *Chairman of the British Dietetic Association, spoke of the training of dietitians and of the difficulties involved in adapting existing trainings so that they may produce well-qualified dietitians fitted to fill the many good posts at present advertised. In particular, she mentioned the problem of deciding, for example, how much chemistry, or, at the other end of the academic scale, how much institutional management the dietetic student should be taught. She stressed the need for the help, encouragement and support of the medical profession both in the training of dietetic students and for the trained dietitian who frequently encounters great difficulties in a profession which in this country is still in its infancy.*

Miss Rose M. Simmonds *said that hospital authorities put the cart before the horse when they trained dietitians to produce special diets for a few individual patients instead of putting the emphasis on efficient catering and good cooking for all patients and staff. Until 1939 diet in hospitals (largely supplemented by patients' friends) consisted of one main meal at midday, the other meals consisted mostly of bread and butter with tea or soup. Light meals for gastric cases were invariably steamed fish and milk pudding. But not all special diets to-day provided adequate amounts of the essential nutrients. Recent analysis of obesity and low-salt diets showed low values of calcium, iron and the B vitamins. This was important because such diets were usually continued for long periods.*

During and since the war it had been found that good nutritive diets could be constructed from the available rations if these were all taken up and if "points" were spent to the best advantage. The only difference between special and full diets should be in their methods of presentation, and by the exercise of a little ingenuity the same foods could be made to appear more varied.

Mr. W. B. Morison spoke on the value of a Food Committee in a hospital. He considered the knowledge that such a committee existed tended to keep all concerned on their toes; in addition it provided a means whereby suggestions and criticism could reach the Governing Body of a hospital through channels such as Staff meetings, Nurses Representative Council and Sisters Council. The secretary superintendent, the matron and the catering officer attended meetings of the committee which included lay and medical representatives. The assistant caterer, the head dietitian and the supervisor of the private-wing kitchens attended and submitted their reports so that all aspects of feeding in the hospital came under review monthly. The medical representatives were most useful and he himself, as Chairman of the Food Committee of the Middlesex Hospital, had received invaluable help from them. For instance he had asked them for a report on the tendency of special diets, and that report resulted in the Board and House Committee being informed that within a comparatively limited time there would be as many special diets as ordinary served to the wards, with all the complications these involved in respect of increased space, staff and equipment.

Dr. David G. Morgan said that in the old days, particularly in the pre-Listerian era, there was hardly a person in hospital who was not swinging a high temperature in the evening. Hospitals got into the habit of not providing cooked substantial suppers for these people as the average patient did not require it owing to his condition. Nowadays with penicillin therapy it was relatively uncommon for more than a few hospital patients to be pyrexial. Their appetites for cooked suppers were, therefore, good and this new demand must be met. He was glad to hear that the training of dietitians of the future must be better adapted for posts in hospital kitchens. In the past they were trained for and handled special diets only. They must, in the future, be capable of catering in its broadest sense and have the necessary knowledge both for the purchase of food and the management of kitchen personnel.

Professor John Yudkin said that the feeding of hospital patients could only be improved by the formation of food committees such as that at the Middlesex Hospital, which had been described. But the desire to form such committees depended largely on the interest of the clinicians, whose training in dietetics was often at present quite inadequate. It was mainly through a body such as the food committee that the clinician was made aware of the importance of food. And so the circle was complete. One could not expect to have a food committee unless the clinicians appreciated the importance of modern nutritional knowledge and yet the best way to teach the clinicians was through a food committee. The only way in which the vicious circle could be broken was by the employment of a far larger number of dietitians in hospitals. The fact that there was a dearth of hospital dietitians was chiefly due to the lack of recognition of their value and of their extensive training. This showed itself in the very low salaries at which many posts were advertised.

Dr. Philip Ellman said that an inferior surgical service would not be tolerated in any good hospital and a similar attitude should be adopted with regard to the dietetic service. It had been pointed out that good diet was as necessary to recovery of health as good nursing, surgery or medicine and, as the Joint Tuberculosis Council (Rep.

of Council on Wartime Diet, 1944) had recently reported, institutional food to-day was universally condemned for its monotony, bad cooking and not infrequently its inadequacy. Not only was a properly planned diet needed for purely physical health but eating was social function reacting on the patient's outlook and, as Sir Jack Drummond had pointed out, it was important that right through the buying, preparing, cooking and serving processes it should be organized scientifically. No hospital of the future could possibly be complete without a representative food advisory committee headed by a catering officer who should have adequate powers and facilities. Such minimum requirements were by no means impossible of fulfilment at the present time for during the war at an emergency hospital which had initially very primitive facilities, a food advisory committee of the hospital with a full representation of medical, nursing and administrative staff was able to overcome what appeared to be insuperable difficulties.

Hospital food in its raw state was generally of first quality. Its subsequent handling all too often reduced it to what was commonly known as "institutional food". With determination and goodwill this stigma should surely be overcome in the future. (See also Ellman P., *Post-Grad. med. J.* (1945) 21, 334.)

Dr. James Watt said that doctors in the main deserved the reproaches of Lord Woolton and Sir Jack Drummond over their ignorance of the dietary required by both patients and staff. There was, however, one type of hospital in which, for at least half a century, dietary as a factor in treatment had been fully appreciated, namely, in tuberculosis hospitals and sanatoria. In them, complaint of monotony, poor cooking or service was sometimes justified, but the adequacy of the diet was seldom questioned. Sir Jack Drummond seemed to infer that the appointment of a competent catering officer with wide authority was enough to ensure the proper dieting of patients and staff. A good catering officer, as had been said earlier, was not necessarily a good dietitian, neither was the dietitian necessarily a competent caterer. Neither of them could replace the physician in assessing the value of dietary in treatment. Dr. Marriott was right in asserting that to carry out his duties efficiently the catering officer must have guidance from a committee, which should include not only himself and the dietitian but also a physician, the matron and the chef and be presided over by a member of the committee of management.

Section of Experimental Medicine and Therapeutics

President—Professor H. P. HIMSWORTH, M.D.

[December 9, 1947]

DISCUSSION: PLASMA PROTEIN FRACTIONS

Dr. R. A. Kekwick (The Lister Institute): *Human Plasma Protein Fractionation.*

During the last ten years considerable advances have been made in our knowledge of the protein constitution of biological fluids and of tissues. These advances have been due chiefly to the application of the improved electrophoresis techniques introduced by Tiselius, in conjunction with the optical systems devised by Philpot, Svensson and Longsworth [see 1].

Although it is possible to isolate proteins by electrophoresis, the scale on which such separations can be carried out at present is very limited, and from this point of view the method can only be used on a research basis. In conjunction with the classical methods for the bulk fractionation of protein solutions, it has proved of inestimable advantage in affording a precise and independent means of controlling and improving the resolution of the methods.

In attempting to separate proteins in a relatively pure condition from a mixture in aqueous solution, there are several variables of which use can be made to establish conditions such that a desired protein can be caused to precipitate more or less completely, leaving others in solution.

The following variables determine the solubility in such a system: pH; salt concentration; temperature; total protein concentration; and when solvents are used, a fifth variable—the solvent concentration.

The separation of proteins has mostly been carried out in very concentrated salt solutions, in the region of 2–3 molar, the salting-out procedure. The disadvantages of this method are twofold. First, the products must be freed from the precipitating salt by dialysis, a procedure difficult to carry out under sterile conditions, a necessary restriction if the product is required for clinical purposes. Secondly, the interactions between proteins and salts appear to be more specific at low salt concentrations, the effects being masked at the concentrations required for salting-out.

If a solvent is used for reducing the solubility of a protein, the electrolyte content can be maintained in the low concentration range where effects are more specific. It is easier to add solvents to protein solutions, whilst maintaining aseptic precautions, than is the case with salt solutions. Finally, the majority of solvents which are suitable for this type of work tend to be bacteriostatic, are volatile and can be removed from the products by freeze drying *in vacuo*, an operation easily performed under sterile conditions. The following solvents have been used in the fractionation of proteins from aqueous solution, methanol, ethanol, acetone, dioxane and ether. All of these solvents tend to produce denaturation of dissolved proteins at room temperature, and other concomitant undesirable effects such as loss of biological activity. Consequently it is usually necessary to carry out such fractionations with careful control of temperature in a range from 0° to –10°C.

The protein constitution of human plasma.—In the electrophoretic examination of normal human plasma five components were originally distinguished: albumin, α , β and γ globulin, and fibrinogen. More recent studies indicate the existence of two α globulins, α_1 and α_2 , and two β globulins, β_1 and β_2 .

The quantitative electrophoretic analysis of normal human plasma shows it to be remarkably constant in constitution. The amounts of the various proteins expressed as a percentage of the total protein are about:

Albumin	α Globulin	β Globulin	γ Globulin	Fibrinogen
55.0	14	13.5	11	6.5

Although the plasma components revealed by electrophoresis display a reasonable degree of electrochemical homogeneity, it is important to appreciate that this does not imply absolute chemical or physiological homogeneity. The wide range of physiologically and immunologically active proteins detectable in plasma is apposite to this point, and also the fact that the electrophoretically homogeneous components are susceptible to further fractionation by solubility methods. Further, the activity of proteins associated with specific biological effects is frequently so high in relation to mass that the amounts present in plasma may be far below the power of resolution of the electrophoresis apparatus.

The further exploration of the possibilities of the fractionation of human plasma proteins with solvents were stimulated by the urgent needs of the war. Although plasma can be dried successfully from the frozen state, and will then under proper conditions retain its properties for an indefinite period, there are certain advantages in the provision of a stable liquid transfusion material.

The alcohol fractionation system [2].—The primary object of Cohn's work was the preparation of pure human serum albumin for transfusion. As the work progressed a secondary objective developed, to separate the plasma proteins other than albumin, into limited numbers of main fractions corresponding as closely as possible with the electrophoretic components. These main fractions then formed the basis of various subfractionations oriented with reference to specific biological activities.

TABLE I.—THE ETHANOL FRACTIONATION SYSTEM

Fraction	pH	% ethanol	Temp. °C.	Ionic concentration
I	7.4	8	—3	0.14
II + III ..	6.8	25	—5	0.09
IV	5.8	40	—5	0.09
V	4.8	40	—5	0.11

Details of the fractionation scheme developed by Cohn are given in Table I, which shows the conditions under which four main fractions are separated from plasma. The quantitative distribution of the proteins present in the fractions is given in Table II.

TABLE II.—DISTRIBUTION OF PROTEINS IN ALCOHOL FRACTIONATION

Fraction	Plasma	I	II + III	IV	V	VI
Albumin ..	33.2	0.2	0.7	1.0	29.0	0.3
α Globulin ..	8.4	0.2	1.8	5.4	0.6	0.3
β Globulin ..	7.8	0.8	6.2	3.1	—	—
γ Globulin ..	6.6	0.5	6.0	0.2	—	—
Fibrinogen ..	4.3	2.6	1.6	—	—	—

Figures are grammes protein from 1 litre of plasma.

Though fraction V is the only one which approaches electrophoretic homogeneity, the others tend to show the predominance of one component. Originally fractions II and III were separated individually, but it was found more convenient to separate them together and then to subfractionate. The subfractionation of II + III provides a second product approaching electrophoretic homogeneity, namely, γ globulin, and by further treatment of fraction I a substantially homogeneous fibrinogen may be obtained. The homogeneity of the albumin, fraction V, can be improved by crystallization.

The ether fractionation system [3, 4].—Ether can also be used as a precipitating agent in much the same manner as alcohol. Details of the system which is less extensive than that for alcohol are given in Table III.

TABLE III

Fraction	pH	% ether	Temp. °C.	Ionic concentration
Fibrinogen ..	7.2	11	0	0.14
Prothrombin ..	5.3	10	0	0.13
Globulin ..	5.3	17.5	-3.5	0.05

The residue after the removal of globulin consists of albumin and residual globulin. This can be frozen with excess ether to remove lipid and can be recovered in this way for use in transfusion. The globulin fraction is subfractionated to provide a fairly pure γ -globulin preparation.

THE CLINICAL APPLICATION OF PLASMA FRACTIONATION PRODUCTS

Perhaps the most versatile of the products of plasma fractionation are fibrinogen and thrombin [5]. Since the clotting time of fibrinogen-thrombin solutions can be accurately controlled, a liquid mixture can be applied locally, which subsequently clots. The tensile strength of fibrin clots, though also a function of other variables, increases with fibrinogen concentration, and solutions of fibrinogen up to ten times (2%) the corresponding concentration in plasma are readily attainable. The clots formed from such solutions have been used to suture severed nerves by a soldering type of process. Rather lower concentrations of fibrinogen provide, with thrombin, an excellent adhesive for the application and fixing of skin grafts, dispensing with the necessity for pressure dressings. Grafts fixed in this manner vascularize with extraordinary rapidity and the tendency to bronze pigmentation appears to be reduced.

Fibrinogen preparations also contain a material which is effective in reducing the whole blood clotting time in hæmophilia from, say, seventy-five minutes to around fifteen minutes. An injection of 10 ml. of a 2% solution will keep the clotting time at this level for about forty-eight hours [6, 7].

Fibrin films, resembling sheet cellophane in appearance, have been successfully used as dural substitute with marked absence of adhesion. The film is eventually replaced by fresh dural growth.

Somewhat less purified fibrinogen solutions are utilized in the production of fibrin foam. By suitable devices, these solutions are beaten to a finely dispersed foam which is set by adding thrombin and then dried from the frozen state. Such foams if rewetted tend to shrink rapidly, but this can be prevented by baking the dried foam at 130° to 170° C.

The dried foam will absorb almost its own volume of thrombin solution, and is used in conjunction with this for local hæmostasis in internal surgery. The foam is allowed to remain in situ following operative procedures, and eventually becomes organized into the tissue without scar formation.

It has been established that the antibodies in many infectious diseases are associated with the γ -globulin of normal adult plasma [8, 9, 10]. Concentrates of this protein containing 15 grammes protein/100 ml. have been very successfully utilized in the control of measles and may be useful in infectious hepatitis. For measles, intramuscular injections up to 5 ml. are required. The use of similar concentrates prepared from convalescent plasma pools from other infectious diseases, for example, mumps, has been examined.

The A and B isohæmo-agglutinins, which appear to be associated with β globulin, have been purified and concentrated from pools of plasma of suitable blood group. High titre sera are required for accurate blood group testing, and concentration methods make available the agglutinins from plasmas whose titre initially is too low.

Purified albumin solutions containing 25 grammes/100 ml. have been satisfactory for transfusion in cases of shock, and hypoproteinæmic œdema.

Further research may indicate the clinical usefulness of other fractions derived from human plasma.

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Dr. Nicholas Martin: *The Electrophoretic Pattern of the Circulating Proteins.*

I. *Introduction.*—Electrophoresis may be defined as the phenomenon of the migration of "particles" in a medium, under the influence of a current passed through that medium. In so far as the phenomenon is related to the density of free charge on the surface of a given "particle", two "particles" or groups of "particles" in which the density of free surface charge differs will tend to separate when subjected simultaneously in the same medium to a current of controlled density.

While the study of this and allied phenomena has progressed vigorously for more than one hundred years [Lodge, 8, Picton, 18, Hardy, 6, Burton, 4], it was the technical advance introduced by Tiselius [21, 22, 23, 24] that enabled the principles to be applied with such success to the study of proteins. Prior to his work two major stumbling blocks existed, the disturbance of the boundaries of the migrating proteins by convection currents arising from the heat produced by the passage of a current sufficient to achieve separation in a reasonable time, and the lack of a convenient means of studying colourless moving boundaries. By the ingenious design of the cell, and by immersing it with the electrode vessels in a thermostatically controlled bath at low temperature, he was able to minimize disturbances from convection and to make sharply defined starting boundaries with relative ease. By adaptation of the Topley Schlieren principle he was able to devise a convenient means of visualizing colourless moving boundaries by following the change produced in refractive index of the medium by the presence of varying concentrations of protein.

II. *Some factors influencing quantitative analysis of the protein mosaic from Schlieren patterns.*—Diagram 1 shows in a highly simplified form the behaviour of a mixture of four proteins having differing mobilities, when, dissolved in a buffer solution, they are subject to the influence of a current of constant density. It demonstrates that in such a system only a limited quantity of the fastest and slowest component may be separated in a pure state, and that the more nearly the mobilities of the individual proteins approach each other, the more difficult it becomes to achieve this separation. Svensson [20], and MacLagan and Bunn [12] have both devised methods of "continuous return" by which more effective separation can be achieved in a single sample.

It is clear that in studying an ampholyte such as a protein, mobility will be affected by the pH of the surrounding medium. Indeed, one convenient test of electrophoretic homogeneity is that the protein isolated should move as one entity when examined over a varying range of hydrogen-ion concentration.

When making quantitative analysis of mixtures of proteins it is essential to take notice of the part played by the ionic constitution and concentration of the surrounding buffer and of the total concentration of protein subjected to electrophoretic analysis. Table I condensed from the literature illustrates the magnitude of variations to be expected from these effects. Further, since when using the Topley Schlieren principle it is refractive increment which is being measured, substances other than proteins, which may migrate with individual proteins, may contribute to the refractive increment attributed to that protein.

TABLE I

TABLE I

Protein conc. as mgs. N/ml.	Alb.	γ glöb.	Ionic conc.	Alb.	γ glob.
4.0	58.4%	9.8%	0.1	55%	7.8%
3.0	57.8%	9.8%	0.2	52%	11.7%
1.5	54.6%	11.4%	0.3	51%	12%
Ionic conc. 0.1%		Protein conc. 2.0%			
pH 8.6 Veronal buffer. Descending boundary.					
Neutral salt	Albumin	α globulin	γ globulin		
LiCl	5.80	4.37	1.32		
NaCl	4.87	3.46	0.93		
NaF	4.78, 4.36	3.14	0.60		
mobilities cm./volts/secs.					
pH 7.7					
Ionic strength of buffer 0.20%					
of neutral salt 0.18%					

Table I from data of Perlmann and Kaufmann [17].

III. *The protein mosaic in the normal subject.*—When normal adult human plasma is examined by the technique at a pH somewhat to the alkaline side of the physiological normal the protein mosaic is analysed into five main groups which are referred to as the albumins, the α globulins, the β globulins, fibrinogen and the γ globulins. The pattern does not differ markedly with sex or age with the exception that the fœtus and the newborn appear to have a relative excess of γ globulin, an excess not mirrored in the healthy pregnant woman. When serum is examined the fibrinogen “peak” is absent but frequently a small ill-defined residuum of material remains, travelling with a mobility intermediate between the β and γ globulins. If the pH of the buffer solution is raised to from 8.0 to 8.6 a globulin designated α_1 globulin may frequently be identified running between albumin and α_2 globulin. These electrophoretic patterns of human serum and plasma are not the patterns of pure protein but of the complexes of proteins with non-protein substances; the albumin fraction may contain carbohydrate and fatty acids—the α and β globulin fractions lipoids and steroids. Recently, a β lipoprotein has been described which contains 75% of lipid [16].

TABLE II

Electrophoretic* analysis			Precipitation† with 22.5% Na ₂ SO ₄	Precipitation‡ with 30% (NH ₄) ₂ SO ₄	Precipitation‡ with 50% (NH ₄) ₂ SO ₄	Precipitation with 60% (NH ₄) ₂ SO ₄
Albumin	..	60%	73% (100)	53% (100)	74% (100)	88% (100)
α_1 Globulin	..	5%	12% (16)	7.5% (14)	9% (12)	11.5% (13)
α_2 Globulin	..	7%	10% (13)	12.5% (23)	8% (11)	—
β_1 Globulin	}	12%	5% (8)	7% (13)	6% (9)	—
β_2 Globulin			—	5% (10)	2% (3)	—
Fibrinogen	..	5%	—	—	—	—
γ Globulin	..	11%	—	—	—	—

Analysis of the soluble proteins remaining after precipitation

* After Dole [5] †Perlmann [17] ‡Svensson [19].

Table II from data of Armstrong Budka *et al.* [2].

Table II shows a comparison of the separation of normal plasma proteins obtained by some of the common salting-out techniques used in routine laboratory procedures, with electrophoretic analysis. The electrophoretic analysis in each case refers to that portion of the protein mosaic remaining in solution. It demonstrates that these salting-out methods do not give a cleavage which corresponds to any exact point on the electrophoretic pattern when normal plasma is examined. In general the proportions of albumin to globulin electrophoretically are some 30% lower than those established by salting-out techniques in normal sera [5]. In sera abnormal with respect to their protein content where entrainment and other physico-chemical factors may complicate the picture, the deviation may be more marked. Thus in acute infective

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Dr. Nicholas Martin: *The Electrophoretic Pattern of the Circulating Proteins.*

I. *Introduction.*—Electrophoresis may be defined as the phenomenon of the migration of "particles" in a medium, under the influence of a current passed through that medium. In so far as the phenomenon is related to the density of free charge on the surface of a given "particle", two "particles" or groups of "particles" in which the density of free surface charge differs will tend to separate when subjected simultaneously in the same medium to a current of controlled density.

While the study of this and allied phenomena has progressed vigorously for more than one hundred years [Lodge, 8, Picton, 18, Hardy, 6, Burton, 4], it was the technical advance introduced by Tiselius [21, 22, 23, 24] that enabled the principles to be applied with such success to the study of proteins. Prior to his work two major stumbling blocks existed, the disturbance of the boundaries of the migrating proteins by convection currents arising from the heat produced by the passage of a current sufficient to achieve separation in a reasonable time, and the lack of a convenient means of studying colourless moving boundaries. By the ingenious design of the cell, and by immersing it with the electrode vessels in a thermostatically controlled bath at low temperature, he was able to minimize disturbances from convection and to make sharply defined starting boundaries with relative ease. By adaptation of the Töpler Schlieren principle he was able to devise a convenient means of visualizing colourless moving boundaries by following the change produced in refractive index of the medium by the presence of varying concentrations of protein.

II. *Some factors influencing quantitative analysis of the protein mosaic from Schlieren patterns.*—Diagram 1 shows in a highly simplified form the behaviour of a mixture of four proteins having differing mobilities, when, dissolved in a buffer solution, they are subject to the influence of a current of constant density. It demonstrates that in such a system only a limited quantity of the fastest and slowest component may be separated in a pure state, and that the more nearly the mobilities of the individual proteins approach each other, the more difficult it becomes to achieve this separation. Svensson [20], and MacLagan and Bunn [12] have both devised methods of "continuous return" by which more effective separation can be achieved in a single sample.

It is clear that in studying an ampholyte such as a protein, mobility will be affected by the pH of the surrounding medium. Indeed, one convenient test of electrophoretic homogeneity is that the protein isolated should move as one entity when examined over a varying range of hydrogen-ion concentration.

When making quantitative analysis of mixtures of proteins it is essential to take notice of the part played by the ionic constitution and concentration of the surrounding buffer and of the total concentration of protein subjected to electrophoretic analysis. Table I condensed from the literature illustrates the magnitude of variations to be expected from these effects. Further, since when using the Töpler Schlieren principle it is refractive increment which is being measured, substances other than proteins, which may migrate with individual proteins, may contribute to the refractive increment attributed to that protein.

Fig. 1 illustrates electrophoretic analysis from two conditions involving an increase in mesenchymal tissue. 1A is from a proved case of Boeck's sarcoidosis and shows an increase in the slower-moving components of the protein mosaic.

1B and 1C are two analyses from cases of myelomatosis, the second on the day of death. Kekwick [7] demonstrated that cases of myelomatosis, indistinguishable clinically, fall into two groups by electrophoretic analysis, in the one group the great increase is in the area of mobility of the β globulins, in the other, in the area of the γ globulins. The cases shown fall into the second group having an enormous increase in globulin, moving with a mobility corresponding to γ globulins. The whole area is closely defined, implying that the proteins indicated by it are moving with a reasonably uniform velocity.

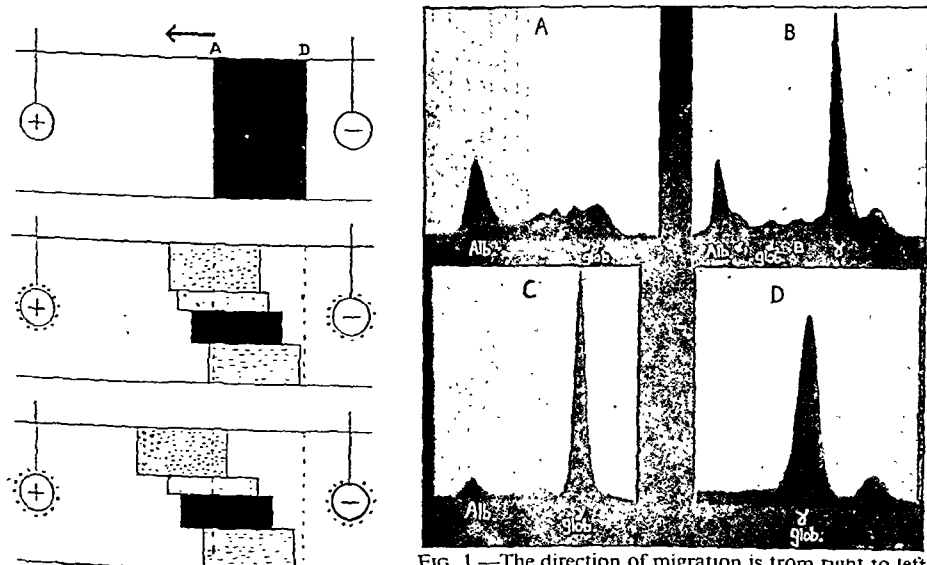


FIG. 1.—The direction of migration is from right to left.

DIAGRAM 1.—The arrow indicates the direction of migration, in this diagram to the +ve pole. The black area in the top diagram represents a solution of four proteins prior to switching on the current. The two "boundaries" between the protein solution and the buffer which separates it from the electrodes are marked A and D. The second diagram represents the state of affairs shortly after the current has been switched on. It will be seen that the most "advanced" boundary is now composed of the fastest moving component of the mixture only. The third diagram represents the position some time after the current has been running. The advanced boundary of the fastest component is well forward, but its "hind" boundary is still overlapped by the forward boundary of the next fastest moving component. It illustrates the limitations of the method in effecting separation of two components of closely related mobilities.

1D represents the isolation of the abnormal constituent from 1B by quantitative electrophoresis. The appearances would suggest that one was dealing with a homogeneous substance with regard to its electrophoretic properties, mobility studies placing it among the γ globulins. However, Professor Oncley very kindly submitted the material to ultracentrifugal analysis and demonstrated that it did in fact consist of three components with different sedimentation constants. At post-mortem proteins resembling the γ globulins were demonstrated in highest concentrations in those tissues most heavily infiltrated by tumour cells, being present in negligible amounts in other tissues. They were not identified in tissues from a normal submitted to parallel extraction [15].

Conclusion.—It cannot be too strongly stressed that electrophoresis is only one of many techniques which have proved of use in studying complex mixtures of macromolecules. Finally electrophoretic homogeneity should never be taken to imply either chemical or biological homogeneity. It does offer an extremely convenient way of analysing complex mixtures of proteins in solution with an accuracy—having regard

hepatitis the difference may be as much as 36% and in chronic liver damage 40% or more (Martin, unpublished data).

IV. *The protein mosaic in disease processes.*—In this brief survey it will only be possible to give a few illustrative examples of the alterations which may be demonstrated in the protein mosaic in disease. It must be stressed that in many conditions, as for instance extreme starvation, striking differences are not discernible by this technique, while in many other conditions the changes demonstrated are those which, with intelligent forethought, one might anticipate. Moreover the changes in pattern when they occur are in most instances not so much a characteristic of the individual disease process as of the host's reaction to that process. That reaction may be the same in conditions which, clinically, differ widely. In nephrosis, electrophoretic analysis demonstrates that the major contributors to the circulating plasma proteins are the α and β globulins [11]. It must be remembered as Longsworth and MacInnes [9] have pointed out that the lipoids, and more especially the cholesterol and allied steroids travelling in loose association with the β globulins contribute largely to the refractive increment demonstrable in that area of the pattern. Both in nephrosis and in obstructive jaundice the plasma cholesterol may be raised and in both these conditions one frequently detects an increase in material migrating with the velocity of the β globulins.

Examination of the urine in nephrosis shows that the protein passed in it is predominantly albumin with some β and some γ globulin [11].

Luetscher [10] studying a carbohydrate-free crystalline human albumin observed that at pH 4.0 it resolved into two components, the faster component contributing about 60% of the total. When the albumin from a nephrotic patient was examined the same resolution was observed but the ratio of the faster to the slower component was reversed. Bourdillon [3] had calculated that the molecular weight of human nephrotic albumin differed from that of normal human albumin.

In diseases involving the liver parenchyma the pattern varies with the stage and extent of the disease. In simple uncomplicated infective hepatitis—in the early stages there is a relative depression of the albumin with increase in the γ globulin. As the patient recovers the albumin tends to revert to a normal level and the circulating γ globulin level to drop. The α and β globulins may show some change, notably between the fourteenth and thirtieth days and it has been observed that their deviation from normal is greatest in those patients having a tendency to relapse [13]. That the actual recovery of the circulating albumin may not be so rapid, as superficial examination of the electrophoretic data would lead one to suppose, is shown in Table III where the total circulating components have been calculated on two

TABLE III

		Total proteins gm./100ml.	Plasma volume ml.	Total circulating protein gm.		
				Albumin	$\alpha_2 + \beta$ globulin	γ globulin
1st week	..	6.5	3,150	105	43	41
4th week	..	7.5	2,550	117	44	24
Normal	..	7.2	3,250	140	45	25

Table III from data of Svensson [20].

analyses in a moderately sick patient, the first toward the end of the first week, the second early in the fourth week during the recovery phase. It will be seen that whereas the level of the γ globulin has fallen to normal limits, the total amount of circulating albumin is still 15% below normal in the fourth week. In established chronic liver damage analyses show an absolute diminution in circulating albumin with an increase in the γ globulin which may represent 30% of the total circulating protein.

Section of Radiology

President—J. S. FULTON, C.B.E., M.D.

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The Serious Limitations and Erroneous Indications of Biopsy in the Diagnosis of Tumours of Bone

By JAMES F. BRAILSFORD, M.D., Ph.D., F.R.C.P., F.I.C.S.

Radiologist, The Royal Cripples and The Queen Elizabeth Hospitals, Birmingham

THE clinical signs and symptoms of tumours of bone are so variable in their manifestations that except in a small proportion of cases they are of little or no value in determining the nature of a bone tumour.

These tumours occur at all ages from birth to old age. They show a great difference in their rate of growth; some ending fatally within a few months, others showing a slow progression over years, and in some cases, after a few years, a retrogression. They occur in patients who exhibit vivacity and all the robustness of the healthy, to patients with the anxiety, wasting and cachexia of the dying. Pain accompanying their growth may be negligible, or so severe that only morphia can give relief. In some cases tenderness may be so exquisite that the patient screams at the approach of the examining hand, whilst in others firm palpation may be permitted without any discomfort.

These tumours are so variable in all their characters and manifestations that they defy any scheme of classification. We should be lucky indeed if we could readily separate the simple from the malignant. They are so rare in any one surgeon's practice, unless he is a recognized authority to whom many of his colleagues refer their cases, that little practical experience in diagnosing and treating these bone tumours can be obtained; yet the general practice is for the surgeon to treat his own cases.

Yet there would appear to be some divergence of opinion as to who should treat these lesions. A contribution to a discussion on the diagnosis of bone tumours by a learned orthopædic surgeon was prefaced by his message: "There is no need for the pathologist or the radiologist to lose one wink of sleep over the diagnosis of a bone tumour for that is the province of the surgeon." These sentiments have recently been re-echoed from America, where Philip D. Wilson [2], speaking in support of the claim that bone tumours are the responsibility of the orthopædic surgeon, is quoted as saying: "I know in several centres there are excellent general surgeons caring for these patients and doing excellent work; yet I know of one instance not long ago when a Brodie's abscess was explored under the diagnosis of neoplasm. It needed exploration, it was the proper thing to do; but it seems to me a knowledge of bone lesions or bone pathology is necessary and certainly will help in the diagnosis. I think these men who are treating tumours will invariably have brought to their clinics a great many cases of non-neoplastic conditions which represent bone anomalies of various types which require orthopædic care. *They will undertake the treatment, when they are not properly qualified for it.*" It is not surprising to see accounts (and hear of many more) of amputations and other mutilations for tumours judged to be malignant, yet proving to be simple. But this does not apply solely to general surgeons or the Cottage Hospitals. Their work is based upon the teaching and practices of our University Hospitals and it is the work done in the latter which we must scrutinize if we are to assess the relative merits of the methods employed.

It is generally agreed that notwithstanding the recognition of the clinical examination as of the first importance this does not permit of the diagnosis of any bone

to the amount of material used—hitherto unobtainable by any means of parallel simplicity.

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Dr. F. O. MacCallum asked Dr. Kekwick if it was known what temperature human serum γ globulin could be exposed to without alteration of its structure and antibody content. If certain viruses as well as antibodies might be present, it was desirable to know how they could be inactivated.

Dr. C. H. Gray, in answer to a question, stated that experiments he had performed in collaboration with Dr. Kekwick suggest that the binding of bilirubin by different fractions of the plasma proteins bears no relationship to the nature of the direct van den Bergh reaction.

Dr. L. F. Hewitt: A matter that tends to be overlooked is the question of the physiological and immunological significance of the plasma proteins. Knowledge of the distribution and physico-chemical properties of the fractions is accumulating but these are only symptoms of the function of the cells which produce the proteins and further knowledge is required of the mechanism of synthesis and site of origin of the plasma proteins. It seems fairly certain that different proteins originate in widely separated organs and cells, but detailed knowledge is lacking of the origin of both normal and pathological plasma protein fractions.

Dr. A. C. Dornhorst: Can Dr. Martin tell us whether bilirubin always migrates with the same protein fraction irrespective of the type of jaundice present? If not, does its behaviour throw any light on the mechanism of the van den Bergh reaction?

Dr. Kekwick, in reply: So far as I am aware no data as yet exist in the literature which would furnish a categorical reply to Dr. MacCallum's question.

Dr. Martin, in reply: I think that our investigation of the γ globulin in the plasma of myelomatosis is the beginning of the filling in of the gap in our knowledge to which Dr. Hewitt refers.

In reply to Dr. Dornhorst it seems probable that bilirubin is capable of combining with more than one protein fraction [14]. The precise mechanism of the van den Bergh reaction still remains to be elucidated.

malignancy. An examination of the reports on the histology of bone tumours reveals the indecision which the appearances produce. For, whereas in the descriptions of normal tissues we see the use of definite terms such as fibrous, cartilaginous, or osseous tissues, in the descriptions of pathological tissue we see the indecisive terms mucoïd, fibroid, chondroid, osteoid, muco-fibroid, fibro-chondroid, chondrosteoid, &c., terms which permit of considerable latitude of expression by different observers.

No more important contribution on this is made than in the latest publication by Platt [1] who used as illustrations photographs (3A and 4A) and photomicrographs (3B and 4B) of two cases; both of them he describes as osteogenic sarcoma of the upper end of the fibula. Both 3B and 4B are described as showing "the predominant cell was oat shaped" yet the photomicrographs present quite different pictures. The photographic appearances are also different; 3A showed the tumour protruding from the fascia at multiple sites as in a malignant growth, but 4A shows a more regular spindle-shaped tumour. 3 was of a patient who "died eighteen months after amputation", 4 was of a "patient who is living 13 years after the amputation". No radiographs of these lesions are produced but the subsequent histories bear out the macroscopic appearances rather than the histology. Several papers describing erroneous histological interpretations of multiple cases have been published by the author [see 10, 11, 12, 14, 15, and 16].

It would appear that students who have been taught with the typical material do not realize how seldom tumour tissue presents characteristic features, and there was good reason for Ewing [4] to state: "Few surgeons realize the limitations in the histological diagnosis of bone tumours and the conditions which simulate or accompany them."

(2) *How Should Biopsy be Performed—By Cutting Needle or Punch, or By What H. Platt [1] Describes as "Real Biopsy, Real Exposure and Removal of Tissue"?*

H. W. Meyerding [5] of the Mayo Clinic has stated: "I do not believe in needle biopsy, but prefer that which includes incision, inspection of the tumour and removal of an adequate portion of tissue for pathological examination." Yet there are many other surgeons who prefer to use a cutting needle or punch to obtain tissue for histological examination.

(3) *Why was Punch or Needle Biopsy Introduced?*

It was held by many surgeons that incision into malignant tumours disseminated the malignant cells through the medium of the cut vessels. Diathermy cutting was hailed with enthusiasm because it was thought that this method of cutting would prevent dissemination of the cells by surgery. Following biopsy a good proportion of patients with sarcoma develop metastases; but then many patients, when first reporting because of a tumour, show metastases, and we cannot say that metastases are not present though radiographs fail to detect them—it requires time before these secondary lesions arrive at a size which permits of radiographic visualization, what I have called [17] "the latent negative radiographic period". But the radiographic appearances before and after biopsy certainly suggest dissemination. We may see changes within the affected bone but no irregularity of the surface before biopsy, but the appearances following biopsy suggest that the bone has exploded at the site, for the bone becomes fragmented and sun-ray spicules appear to shoot out in all directions.

We know that surgical exploration of the affected area in the acute phase of scurvy or myositis ossificans results in considerable extension of the ossific cells for this has been demonstrated radiographically on many occasions; see S. L. Baker's illustrations [6]. It results in further invalidism and more permanent and extensive damage. Surgical incisions, and particularly the removal of large pieces of tissue, tend to destroy the scaffolding on which repair will be laid down if the lesion proves to be

tumour in its early stages. As Bloodgood stated: "In former years when malignant disease could be recognized clinically there were no cures." Consequently, even the orthopaedic surgeon must look elsewhere for evidence. Because the histology of normal tissues is characteristic, and pathology is associated with very marked changes, to histology we turned for conclusive evidence. Though there is considerable ground for distrusting the interpretation of histological appearances, a widespread belief prevails in the infallibility of histological evidence. So firmly is this belief held that if the subsequent history of the case differs from the forecast given, it is the pathologist, however eminent, who is blamed for the erroneous interpretation, rather than the vagaries of the histology.

Certain leading authorities hold that biopsy affords the means for fully proving the nature of bone tumours and always resort to biopsy prior to any major surgical measures. Most radiotherapists act likewise. Thus recently Platt [1], reviewing 161 cases, claims 23 five-year survivals, and states: "Twenty-two of these patients treated by radical operation are *fully proven cases*, but in one, a pelvic sarcoma, *proof from biopsy* was not forthcoming." "Forty-one patients in this series of short survivals died within a year of operative treatment. At first sight this is a melancholy picture, but when we consider that in 128 accessible tumours treated by radical operative procedures, 79 patients have survived over two years and 23 of these five years and more, the current view, *that the general outlook on bone sarcomata as a whole is by no means tragic*, is reinforced." Have we any right to reinforce this outlook?

LIMITATIONS OF BIOPSY

If the infallibility of biopsy could be substantiated, the risks of anaesthesia, surgical exploration and all that it means in additional damage, dispersal of tumour cells, &c., and the mental and physical pain caused thereby—I can recollect two deaths which took place within a short time during biopsy on what proved to be simple lesions—could possibly be regarded as negligible or at any rate justifiable. Before we resort to biopsy we should satisfy ourselves with satisfactory answers to the following questions:

(1) *Can the Findings of Biopsy be Relied Upon?*

L. C. D. Hermitte and F. Ellis state [18]: "The diagnosis of the true nature of a tumour (particularly of a neoplasm) must finally rest upon histological evidence." Microscopical examination of animal tissues reveals that the normal tissues have a characteristic cellular structure which permits us to identify them. The histologist, Reichart, promulgated the concept that bone, cartilage, tendon, fibrous and elastic tissue, derived from the mesenchyme, are all adaptations of, or developments from, the primitive connective tissue. Subsequently Leriche and Policard [3] brought forward evidence in support of their suggestion that these mature tissues may be induced, under certain influences, to revert to their primitive state and then undergo ossification. Not only can the mature normal mesenchymatous tissues be recognized readily from their microscopical appearances, but abnormalities in their size, shape, disposition and staining features also. Certain bone tumours present striking histological features as they do radiographic features, which may be regarded as typical indications of malignancy, and it is the material from these which is used for teaching purposes because the abnormal features are so striking. Unfortunately for diagnosis some of the cellular features which are regarded as characteristic of the malignant lesion are found under certain circumstances in tissues of a simple nature, but, on the other hand, they may be absent from the tissue of the frankly malignant tumours. This was appreciated by Ewing [4] who stated: "In the average specimen of callus the proliferative activity of fibroblasts, osteoblasts and endothelium is quite remarkable and often presents a picture which is difficult to separate from sarcoma." Histological preparations of bone tumours have been submitted to multiple pathologists who have given reports on them which in any one case have varied from simplicity to high

spaces containing loose connective tissue. *There is little evidence of tumour growth and none of malignancy.*

"19.4.47: Patient readmitted to hospital as tumour mass has recurred. Radiograph revealed extension of growth. ? sarcoma.

"21.4.47: *Operation* (3rd).—Exposure of lower end of femur—large sarcoma found at lower end of femur. Portions sent for biopsy. Report of Pathologist: 'Sarcomatous changes in neoplasm at lower part of right femur. *Chondrosarcoma of femur.*'

"24.5.47: *Operation* (4th).—Disarticulation at right hip-joint. Patient made a good recovery and was sent home to await an artificial limb."

Note that *this patient had four anæsthetics and surgical explorations* and that the interpretation of simplicity of the histological material at the first biopsy and even after the second resection of the whole mass was erroneous, though there was already a radiographic interpretation of malignancy.

The second case was published by S. L. Baker [6] (his Case 1):—

A boy aged 4½ years: "15.7.41 slipped on the floor and sustained a spiral fracture of the mid-shaft of the right femur for which he was admitted to hospital. A mass developed in relation to the fracture site, within four weeks this had reached a considerable size and in an X-ray taken on 11.8.41 the central part around the fracture showed much calcification and a layer of new periosteal bone could be seen extending from this up the shaft. By this time the thigh was greatly enlarged, felt hot and showed many distended veins and the appearances so closely resembled a rapidly growing sarcoma that a biopsy was performed on 19.8.41, five weeks after fracture. *Disarticulation at the hip-joint was considered but regarded as too risky and of doubtful value and palliative treatment was decided on.* A note made at this time 2.9.41 remarks: 'Huge swelling of right thigh from below knee to above groin, œdematous, hot, distended veins on surface. *Tumour fungating through biopsy scar.*' X-ray treatment 3,000 r spread over three weeks was given between 4.9.41 and 26.9.41. The mass in the thigh gradually became harder and the biopsy incision healed. About this time I was shown a section which at first I considered showed a chondrosarcoma but later had expressed doubt upon. An X-ray taken 7.6.44, nearly three years after fracture, shows that the callus had been largely reconstructed and now formed part of an expanded but porosed and trabeculated femur shaft with no signs of the fracture site."

He comments on this as follows: "Chondrosarcoma was, I think, not an unjustifiable diagnosis. Had the leg been removed in my Case 1 *it would have been impossible to prove that it was not a sarcoma cured by amputation.*" But considerable doubt could have been thrown upon the diagnosis by reference to the author's previous paper [8] and, in view of the proved nature of the lesion, the record "Tumour fungating through the biopsy scar" would appear to be inaccurate. That it was a *real biopsy* is indicated by the recital of descriptions of the material, i.e. "The material consisted of several pieces of tissue, some measuring as much as 4 cm. by 2 cm. by 1 cm."

(5) *Does any Form of Biopsy Permit us to Watch Sufficiently the Evolution of a Tumour and to Establish its Nature?*

Biopsy is unlikely to be considered until one or two months have elapsed since the onset of the lesion. During this interval, though there may be little clinical and no radiographic evidence of bone involvement, considerable changes can occur in the tissues, the inception and nature of which the histologist appears to be unable to divine from the material taken after the interval. In the second case cited, S. L. Baker [6], though fortunate enough to have clinical and radiographic evidence of a definite fracture but five weeks previously, was unable to indicate the true nature of the lesion. He regarded the abnormal tissue in the first instance as that of chondrosarcoma and later (owing to the good fortune of the child being too ill for disarticulation at the hip-joint), when resolution was obviously occurring, as hyperplastic callus, which he stated at a recent meeting began with the deposition of woven bone. Commenting in his paper on a previous report of the author's on four such cases he states: "I have been unable to find any detailed account of a closely similar case in the literature. Brailsford (1943), however, gives an account of the radiographic appearances of four cases of osteogenesis imperfecta in which masses of bone were found in relation

of simple nature. It certainly introduces the definite factor of trauma, the results of which may seriously affect and confuse the radiological, clinical and histological picture. Hence it was thought that tumour tissue could be removed with the minimum trauma by needle puncture biopsy.

(4) *Why "Real" Biopsy?*

Because it was thought that needle biopsy or mere incision into the tumour and removal of a small portion did not provide adequate material for diagnosis. Indeed, in the "Recent Advances in Clinical Pathology", 1947, speaking in support of aspiration biopsy, Hermitte and Ellis make the following statement: "Failure to obtain any tissue is of little significance, and failure to obtain pathological material does not rule out the presence of a lesion. It is in fact the rule in the case of hard lesions, such as fibromas, and well-differentiated bony osteogenic sarcomas. It is worth remembering, however, that a negative result, in cases such as those mentioned, far from being devoid of meaning, may indeed be considered as evidence in favour of a reasonably confident clinical diagnosis." The reports on the small fragments of tissue often resulted in erroneous opinions being given. It was thought that extensive exposure of the tumour permitted the surgeon to obtain adequate pieces of tumour from several sites which he regarded as likely to supply the essential evidence, and J. S. Young [7] had expressed his opinion that incision into the tumour bone would release the tension which possibly results in the expulsion of tumour cells into the vessels.

But even when the whole tumour is resected or the affected limb amputated, permitting the pathologist to cut out sections where he will, we still have the experience of erroneous interpretation of well-established lesions; sometimes malignant lesions being described as simple, sometimes simple described as malignant.

The histories of the following two cases illustrate these errors. Details of the first case are as follows (notes supplied to author from case history):

"The patient, K. P., a young woman aged 20, attended hospital complaining of progressively increasing pain in the lateral aspect of the right knee-joint—a site in which she had noticed a swelling which had steadily increased in size during the past two years. She could give no history of injury or strain to the area. No abnormal features were detected in the clinical history or examination apart from this.

"On examination the right knee appeared to be swollen on the outer side. On palpation a bony swelling was felt on the lateral aspect of the lateral femoral condyle which was about 3 in. long and 2 in. wide reaching to the lateral edge of the patella. The surface was smooth and edges were obscured by soft tissue. The mass appeared to be attached to the bone but not to the skin. Tenderness was present at one point only about the centre of the mass. There was no free fluid in the knee-joint and though flexion was limited to 90 degrees the other movements were full. The inguinal glands showed no enlargement. Radiographs, 12.7.46, showed a large mass of calcification situated on the posterior and external surfaces of the lower third of the femur. The bone does not appear to be eroded at any place and shows a well-marked line of demarcation. The nature of the lesion is uncertain but it would not appear to be a bone sarcoma. The possibilities are myositis ossificans or chronic inflammation and a simple bone tumour. No lesion revealed in the chest or other bones by radiography.

"October 12, 1946: The radiographs were sent to Dr. James F. Brailsford, Birmingham, for his opinion, and his report dated October 13, 1946, reads: 'I am of the opinion that this is a chondrosarcoma of relatively slow growth. The characters and clinical features are against your suggestion of melorheostosis.'

"4.11.46: *Operation (1st)*.—Biopsy of bone tumour. Specimen sent to Edinburgh for examination and report.

"21.11.46 (Report on biopsy material): 'No evidence of malignancy and no evidence of osteogenic sarcoma. I do not know what all these appearances mean in terms of cell metabolism but since this was a tumour I think it can only be a chondroma which is undergoing ossification. I have shown the slide to Professor Flanery who confirms that there is no evidence of sarcoma and agrees that ossifying chondroma is the most reasonable histological diagnosis.'

"25.11.46: *Operation (2nd)*.—All the tumour removed as far as possible.

"8.1.47 (Pathologist's report): 'Microscopic sections show cancellous bone with widened inter-

(6) *Does Prompt Amputation Ensure Cure?*

We have no definite evidence that it does. We have evidence that following amputation of limbs because of lesions thought to be sarcomatous, the patients suffer no recurrence, but as I have illustrated [10] with a number of cases the clinical and radiographic features may be judged to be those of sarcoma yet the real proof that they are not was given in the complete resolution of the lesions and restoration to normal health—amputation being put out of the question by the serious condition of the patients at the time. This clinical evidence is surely better evidence than histology of the nature of the lesion, for have we not the evidence of S. L. Baker's [6] case of a hæmatoma mistaken for sarcoma from the clinical, histological and radiographic evidence and his statement that: "Had the leg been removed in my Case 1 it would have been impossible to prove that it was not a sarcoma cured by amputation."

I have previously recorded two cases in which erroneous interpretation of histological material may have ended in disaster (*Proc. R. Soc. Med.*, 1947, 40, 787).

In another early case where I was satisfied from previous experience that the lesion was a sclerosing osteogenic sarcoma and that there were no indications of metastases in the lungs or other bones from the radiographic appearances, I advised prompt amputation [12]. This was performed by A. M. Hendry without any preliminary trauma or biopsy. The patient rapidly recovered from the operation, but in little over a year she had hæmoptyses, and radiography showed multiple metastases from which she died within a few weeks. Though radiographs are taken of the lungs or skeleton (metastases from osteogenic sarcoma often develop in other parts of the skeleton before they are recognizable in the lungs; the latter being a terminal event) and fail to reveal any evidence of metastases, this is no proof that they do not exist; they have to grow to a sufficient size or produce sufficient contrast density or destruction, before visualization by radiography is possible—the latent negative radiographic period [17]. This may be as long as a year or more, but may be within one or two weeks. As John Hunter observed: "To amputate is to mutilate a patient we cannot cure. It should therefore be considered as an acknowledgment of the imperfection of our art." Though amputation does not ensure cure it removes all chance of investigating the nature of the lesion and its response to various forms of treatment, i.e. it contributes nothing to our knowledge of bone tumours.

(7) *Will Biopsy Enable Us to Get an Early Diagnosis?*

We have seen from the histories of the cases cited that the evidence supplied by biopsy may indicate simplicity when the lesion is malignant or indicate malignancy when the lesion is simple, and that prompt amputation in early cases with little or no reliable signs may prove to be unjustifiable, yet when the evidence of histology is reported as simple great delay may result, as in the first case cited. Though in this case the radiographs permitted the diagnosis of malignancy to be made the patient was submitted to four surgical operations and a delay of seven months because the evidence provided by biopsy, and later extensive resection, was of a simple tumour.

(8) *If the Histology is Reported as Indicating Malignancy Would the Surgeon Promptly Amputate a Limb for an Early Lesion which on Clinical and Radiographic Grounds is Uncertain? If he Would Not, What Can Justify the Surgery of Biopsy?*

Amputation would result in the destruction of limbs for many simple lesions, which, as I have shown [10], left alone, would resolve. Even when the evidence of clinical, radiographic and histological examinations has been interpreted as indicating a malignant tumour, it has been found that the lesion was simple; see cases cited under question 6.

(9) *Does the Evidence of Trauma Assist in Diagnosis or Influence Biopsy?*

It does and it should. The author makes it a rule to regard any lesion as simple in the first instance if there is definite evidence of trauma and the radiographic evidence

to the femur. He gives an illustration of the X-ray appearances of one of these showing involvement of the lower two-thirds of both femurs in masses of spongy bone very similar to the end-result seen in Case 1 here reported. He assumes that this condition resulted from subperiosteal hæmorrhages produced by scurvy, but the evidence for this conclusion appears very scanty, and the right femur shows a bend suggesting an old fracture in the lower third of the shaft and also an irregular mass of bone extending into the soft tissues from the upper half of the shaft. One of the other three cases he mentions was a boy of 14 years who showed a cancellous mass extending from the lesser trochanter down the whole length of the diaphysis of the right femur. This developed after a contusion of the thigh seven years previously. It appears to me that all four of Brailsford's cases may well have been traumatic in origin, with, quite possibly, incomplete fractures which passed unnoticed at the time. In one of these four cases Brailsford noted that there was also a mass on the lower end of the right tibia and that this underwent a rapid increase in size and showed evidence of malignant metaplasia; it may have been a rapid callus production following trauma to the masses." The evidence of malignant metaplasia in the one case was a change in the radiographic appearances and death later with metastases.

Unfortunately Baker did not seek further information respecting my cases before he published his paper, which was not seen by me until it was brought to my attention by a colleague some months after. I could then have indicated that though infantile scurvy is usually regarded by the authorities as a deficiency disease which shows itself between the eighth and twelfth month, I have seen instances of infants within the first three months of life with large hæmatomata enveloping the whole of one or more diaphyses which began to improve immediately, clinically and radiographically, on the administration of vitamin C and maintained freedom from recurrence. There is no necessity for the trauma to be of such severity that fracture is produced to cause a hæmatoma, though in osteogenesis imperfecta fracture may occur merely from turning over in bed. That the initial lesion was hæmatoma and not deposits of woven bone is supported by R. Hutchison and A. Moncrieff [9] who have pointed out that "the chief changes (in infantile scurvy) are in the neighbourhood of the bones. A section made across a limb at the site of a swelling shows that the periosteum is hypervascular, thickened and separated from the subjacent bone by a layer of partially organized blood clot. There is no sign of inflammation and no hard bone is formed in the periosteum, except in long-standing cases". In one case seen by the author there was radiographic evidence that the hæmatoma, which when seen first when the child was 3 months old, contained a deposit of amorphous calcium, had begun to ossify within one month of the regular administration of vitamin C.

Repeated biopsies are likely to lead to further confusion, for added to the initial lesion you have the effects which have resulted from the surgical trauma some weeks or months previously. Though "real biopsy" may permit of macroscopic examination of some aspects of the tumour, but not all, such extensive inspection would hardly be reasonable, or even possible, at the subsequent operations and the material provided for histological examinations can be but a microscopic portion of the whole tumour; and even when multiple sections are taken they may not include the features essential for accurate diagnosis, and do not permit of visualization of the tumour as a whole, or permit us to watch its development—facts which are well illustrated by S. L. Baker's case [6].

Ossifying hæmatomata, not only in scurvy and osteogenesis imperfecta, but also in limbs with neurovascular disturbances and in hæmophilia, and even at the site of unsuspected fractures, have been mistaken on their clinical and histological evidence as sarcomata and amputation has resulted when the patients were considered to be fit enough to stand the operation. Undoubtedly some of these cases are regarded as "cures by amputation".

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which are essentially different. Not all observers are sufficiently careful in describing what they see. Unfortunately it happens that these erroneous interpretations are the ones which often attract interest, and later writers, perhaps equally careless, apply such descriptions to material of their own, so that we ultimately get lesions described which are totally different from those in the original work. The author has successfully established the erroneous interpretations recorded in several such cases in others. However, criticism of such accounts is difficult because it may be felt that all the facts have not been included.

RADIOLOGY

With the unsatisfactory nature of the evidence provided by biopsy we must turn elsewhere for better evidence and I believe that this is being supplied with increasing accuracy by radiology.

John Hunter observed: "It is astonishing to see what little curiosity people have to observe the operations of Nature and how very curious they are about the operations of art," though he had not the advantage of radiological examination by which it is possible to watch the changes taking place in the tumour and the bone in which it is growing. We have seen that there is little to be gained by precipitate amputation, but something is to be gained by observation over a period when the radiographic evidence at the first examination is not conclusive. As soon as Roentgen's discovery was made known to the world it was hailed by the medical and lay press as a means of examination which could be done without causing the patient pain. Radiology contributes its greatest help in the diagnosis of bone tumours when used in this way. Unfortunately instead of using X-rays in this way, watching the development of lesions, and learning the time-table of the changes in their radiographic appearances, there has been an incitement to biopsy, a tendency to seek a rapid explanation for the radiographic appearances, particularly when they are spectacular, by biopsy. This as we have seen inflicts pain and risk without necessarily contributing any useful additional information and often providing confusing evidence and complications. It is this outlook which entices the enthusiast, the thoughtless, and the inexperienced, to cut into the tissues of a patient who is already suffering from a lesion which clinically and radiographically is inoperable—a procedure which cannot reasonably be justified. It is amazing how some of these apparently inoperable lesions will completely resolve when surgery is considered and left quite out of the question; meddlesome interference often obscures the issue, delays resolution, and may prevent complete restitution. I have shown in my book [14] that radiographic appearances of most bone tumours are characteristic and permit of classification but the evidence is not self-explanatory. The significances of the appearances can, like all other studies, only be appreciated fully by those who are prepared to spend the time in acquiring a knowledge of every possible change which can occur in bones and joints, and even when they have done this for many years, they will still be faced, in a big hospital department, with some problem every week. It is because this is not appreciated, even in teaching schools, that we so often see accounts of some simple lesion "simulating sarcoma". These cases will grow less and less as we learn more and more of the characters in radiographic appearances.

In a previous paper (*Proc. R. Soc. Med.*, 1947, 40, 787) reference is made to the opposing indications of radiography and histology illustrated by Geschickter and Copeland.

While it is appreciated by many that before we can detect the early signs of pathology we must have a very searching knowledge of the normal, it is not quite so well appreciated that all the many simple changes in bones and joints must be known before we can hope to distinguish successfully the simple from malignant. Serial radiographic studies of all lesions permit us to draw up a time-table of changes and the knowledge,

is such as could have been produced by the trauma. Obviously this demands a knowledge of the time-table of radiographic evidence of bone lesions and the ability to assess whether the bone was normal at the time of the injury. The development of a sarcoma at the site of a recent trauma, and as the result of that trauma, is very, very rare. I have never seen one (I have seen but two genuine sarcomata arising at the site of old bone injuries. In both cases I reported only the evidence of old fractures—gun-shot wounds several years old—the evidence of malignant metaplasia was indicated by the clinical appearances). Because of this and the experience with biopsy I always advise that lesions with a history of recent trauma and radiographic evidence of changes which could have been produced by that trauma should be treated with medicaments as inflammatory, notwithstanding certain radiographic features which may arouse the suspicion of malignancy. I also advise “no biopsy” for the reasons already stated. In the case of S. L. Baker’s [6] Case 1 the clinical and radiographic evidence of recent fracture should have prohibited the biopsy which was made but five weeks after the fracture. Alas! it did not, and though the subsequent radiographs he used to illustrate his paper showed great extension of the enveloping femoral hæmorrhage due to the surgery, this did not prevent similar disastrous surgery in his Case 2. The catastrophes which may follow erroneous interpretation of malignancy in such cases should warn any surgeon against biopsy.

(10) *Does Biopsy Permit Us to Describe Cases as “Fully Proven”?*

The answer to question 6 suggests that it does not. This is supported by the photograph fig. 2A and radiograph fig. 2B of H. Platt’s cases. The radiograph 2B shows an osteolytic lesion of the upper end of the tibial diaphysis with involvement of the epiphysis (the growth cartilage commonly acts as a barrier to sarcoma) but these clinical and radiographic appearances, though highly suspicious, are no more typical than in the cases which I have recorded which completely resolved without any surgery; and we have the support of his subsequent findings, that this boy is living and well ten years after operation.

Meyerding [5], an advocate of biopsy, goes as far as to state “that even though microscopic section and examination, and roentgenographic examinations are employed, the true characters of the lesion may not be known until *metastases and death have occurred*”.

It is interesting to note that in his 161 cases of sarcomata Platt has no five-year cure from a sclerosing sarcoma and but 4 with a survival of less than two years, yet Geschickter and Copeland [13] claim 17 cures in 65 cases. They state “the chances of cure are more than 25%, when primary radical operation is performed”. It was a sclerosing sarcoma which recurred though prompt amputation followed early diagnosis, see answer to question 6.

(11) *Has Everything Else Been Done to Determine the Nature of the Tumour?*

One thing is certain. Before we seek the help of the pathologist we must make a thorough investigation into the clinical history, signs and symptoms, using all the necessary clinical methods for the detection of sepsis, syphilis and other inflammatory and blood disorders. Though the information obtained in this way may not in itself permit us to determine whether the lesion is simple or malignant, it often gives us an important clue to the diagnosis. It may indicate the directions in which further investigations should be made, or, combined with the radiographic appearances, permit of accurate diagnosis.

There is very great need to scrutinize cases reported in the literature. This particularly applies to reports on groups of cases, for in the enthusiasm to swell the numbers reported on, or to add to some recently discovered signs, cases are included

is indefinite, is erroneous; actually it may directly and indirectly add conflicting evidence which will delay the accurate diagnosis.

Ultimate resolution of a bone tumour which had clinical and radiographic (and even histological) appearances of malignancy is the best evidence of simplicity or removal of the destructive influence. In view of the not uncommon occurrence of such cases, it is unjustifiable to record lesions as "fully proven" malignant tumours, though the clinical, histological (and perhaps the radiographic), appearances suggested malignancy, if amputation results in cure.

A malignant bone tumour, like a gumma, appears to indicate a local expression of a constitutional disturbance, which may completely disappear when the patient is given the essential corrective; for in spite of the earliest amputation similar lesions (? metastases) may develop at any time after, even with twenty years' symptomless interval. Yet as the author has illustrated [10] primary lesions and the multiple associated lesions which have the features of metastases may resolve completely or sufficiently to permit of the average duration of symptomless normal life, i.e. not just an extended existence, which too often is unrecorded in the accounts of two to five year cures. The remarkable response of carcinomatous metastases from some primaries in the breast or prostate to stilboestrol within a few weeks gives us the hope that some such hormone will be found to cure sarcoma.

RECOMMENDATIONS

In the investigation of any bone tumour a careful study of the clinical history and condition of the patient should be made, paying particular attention to any hereditary dysplasia or dystrophy, the possibility of any vitamin deficiency, endocrine or blood disorder, infection or trauma.

A careful radiographic examination should be made of the lesion, of the lungs and any other part of the body which on examination or report is abnormal.

If the radiographic appearances indicate a simple lesion the appropriate treatment should be given.

If the lesion has the radiographic features which suggest malignancy the only treatment which our present imperfect knowledge dictates is amputation. This is an irrevocable procedure, the success of which cannot be predetermined, for we have no means of ascertaining how extensive or widespread the disorder, or knowledge of what can influence it. Consequently as the radiographic appearances can be closely mimicked by inflammatory or deficiency and other disorders, in any doubtful case it would be reasonable to give a course of appropriate medication, and if this fails to produce a favourable response, a course of deep X-radiation therapy. Though Platt has stated: "Irradiation is admittedly a useless form of therapy in tumours of the osteogenic sarcoma group" since the author has shown that some tumours which are indistinguishable from this group completely resolve following X-radiation, the latter is worth a trial. Even when it is established beyond all reasonable doubt that the tumour is malignant and amputation is decided upon, there appears to be some justification in preceding this with a full sarcoma dose of X-rays in a short time, since the radiographic indications of malignancy in certain tumours often disappear for a period following X-radiation therapy [11]—evidence which suggests the possibility of some degree of localization.

Under the auspices of the American College of Surgeons, a Registry of Sarcoma was set up, which included such competent authorities as surgeons, physicians, pathologists, and radiologists. Such a body examines material submitted and attempts to classify the tumours and record the results of treatment. Such a body is necessary where the material is widespread yet locally relatively rare. The author in 1936 [15]

obtained without causing the patient any pain, will permit of more accurate diagnosis and better treatment of the patient.

Not the least value of radiography is its use in watching the progress of a lesion after the exhibition of chemical and physical agents. The response seen by radiography to follow antisyphilitic medication is a better indication of the nature of the lesion than can be obtained by the Wassermann reaction.

If radiology is to hold the place which I believe it deserves to hold, radiologists must shoulder the responsibility, though this will cause the loss of many winks of sleep, but their loss may be rewarded by the desire to possess a sounder knowledge of radiology. Too often in the past have reports been inconclusive, trusting that a biopsy will be made which would supply evidence agreeing with one of the tentative suggestions made and giving the clinician little or no guidance in treatment on which he can rely. It is frequently said that there are few radiologists who can give a reliable opinion on bone tumours and this is why reference is made to biopsy, but I am convinced that the histological evidence is at least equally unreliable and it falls far shorter because it does not permit of visualization of the whole tumour or permit of repeated observations during its growth and treatment. A summation of unreliable reports does not ensure accuracy. While the surgeon, faced with the problem of what to do after making the diagnosis of a sarcoma, sometimes on inadequate evidence or knowledge, either amputates the limb or takes refuge in the transference to his colleague, the radiotherapist, the latter appears to accept as final the report on the biopsy and administers his doses hopefully but not necessarily wisely. More careful clinical and radiological investigation of these cases will reduce the number of cases cured by amputation to the advantage of the patients.

CONCLUSIONS

The essential point to establish in the diagnosis of a bone tumour is whether it is simple or malignant. Attempts at classification on histological appearances are of academic rather than of practical importance—they tend to cause erroneous interpretation. Certain simple lesions, which undisturbed completely resolve, have histological appearances liable to be erroneously interpreted as evidence of malignancy; yet this evidence cannot be obtained without biopsy or more extensive surgery. This cannot be done without causing the patient mental and physical pain, or without subjecting the patient to the risks of an anæsthetic, complications, and the possibility of erroneous interpretations. Though there are certain histological features which appear to indicate malignancy, these features are frequently not found in malignant tumours and the erroneous interpretation of simplicity is made.

The radiographic appearances of bone tumours are infinite and consequently not self-explanatory. The simple lesions have characteristic radiographic appearances which can be verified by serial radiography without causing the patients pain or subjecting them to any risks. The malignant tumours have certain characteristic features also, but their identification necessitates a knowledge of the infinite varieties of the normal and the simple lesions, because these features are mimicked by certain simple lesions. Fortunately the diagnosis can be checked during an interval of careful clinical observation and serial radiography.

Since amputation at the earliest possible moment does not ensure cure of a malignant tumour, and since we have no means of telling whether metastasis has occurred (the radiographic visualization necessitates a long latent period [12]), there is little to be gained by precipitate amputation, but much to be gained by clinical and radiographic study. The supposition that biopsy will permit the surgeon to establish the nature of a lesion, which clinically and radiographically to competent observers

Section of Neurology

President—C. WORSTER-DROUGHT, M.D.

[December 4, 1947]

DISCUSSION ON THE ELECTRO-ENCEPHALOGRAM IN ORGANIC CEREBRAL DISEASE

Dr. W. Grey Walter: Electro-encephalography has been used for about ten years to help in the diagnosis and prognosis of cerebral disease. The advances which have been made in that time are really rather disappointing, but during the war years the rate of progress was slow, though the number of centres increased in all countries.

For the purposes of this discussion the subject may be divided into three parts. First I should like to mention the technical advances which have been made and are now in progress, with particular reference to their value in studying organic conditions. Secondly, I propose to enumerate the empirical findings which are generally supposed to suggest the presence of organic pathology. Thirdly, it may be of interest to scan the methods which are now being developed to extend the scope of the subject.

The basic technical device which has been generally adopted is the employment of multi-channel direct recording instruments, with soundly planned bipolar electrode placements. The general acceptance of this technique is embodied in the recommendations drawn up in this country, in the United States and, more recently, by the International E.E.G. Committee.

In the early days of electro-encephalography, few centres used more than three channels of recording. Nowadays six is the preferred number; some centres use eight and one or two as many as twelve. It is generally agreed that the use of more than six recorders puts a great strain both on finance and on the interpretative ability of the recordist. For this reason a logical development has recently been introduced which can employ several score of channels without burdening the operator with yards of record. This device, which has been called a "Toposcope", exploits the fact that for certain purposes the information required about the patient is more a matter of topographic detail than of changes with respect to time. Accordingly, the electrical activity of the brain is displayed upon a cathode-ray oscilloscope of large diameter in such a way that the regions where electrical activity is in progress can be directly observed as a flickering light, giving the illusion that the observer is looking at the head of the patient and can see the significant discharges where they are actually occurring.

suggested that this should be done in this country. Since then the British Orthopaedic Association made a tentative effort at this but as the Association did not seek the co-operation of general surgeons, pathologists or radiologists its efforts were bound to be ineffective. More recently the Royal College of Surgeons has set up a Registry, but as it appears to base its findings essentially on the clinical and histological appearances without the co-operation of those physicians and radiologists who have studied the problem, it cannot meet with the success which is so desirable. It may provide much material for the museum but lesions so extensively developed that amputation was performed are unlikely to provide much evidence which will assist in what we most desire, i.e. early diagnosis. The pathological museums of the world contain many hundreds of such specimens but they have not materially helped us to make an early diagnosis. Many of the tumours will be from patients who have been subjected to medication, X-radiation, surgical trauma, &c., and these factors acting over a variable time would have had an influence on the histological appearances which cannot be estimated. Though some satisfaction may be felt in contributing specimens to the museum, a greater satisfaction is felt when a lesion completely resolves which had the clinical, radiographic, and even the histological features of malignancy. What we need is a central court of reference which invites full co-operation to which the available evidence of doubtful cases can be submitted for diagnosis before surgery, for from it we may derive the greater satisfaction. In considering the histological classification of any specimen of an amputated limb it would always be well to bear in mind the words of S. L. Baker on a lesion which was proved radiographically and clinically to be an ossifying hæmatoma: "Had the leg been removed in my Case 1 it would have been impossible to prove that it was not a sarcoma cured by amputation".

My thanks are due to the many colleagues who have submitted cases to me and in this instance particularly to Dr. Patricia Franklyn, Dr. Whateley Davidson, the medical staff of the Royal Cripples Hospital, and the members of the X-ray staff for supplying radiographs and case-histories from which the evidence presented has been obtained.

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Section of Neurology

President—C. WORSTER-DROUGHT, M.D.

[December 4, 1947]

DISCUSSION ON THE ELECTRO-ENCEPHALOGRAM IN ORGANIC CEREBRAL DISEASE

Dr. W. Grey Walter: Electro-encephalography has been used for about ten years to help in the diagnosis and prognosis of cerebral disease. The advances which have been made in that time are really rather disappointing, but during the war years the rate of progress was slow, though the number of centres increased in all countries.

For the purposes of this discussion the subject may be divided into three parts. First I should like to mention the technical advances which have been made and are now in progress, with particular reference to their value in studying organic conditions. Secondly, I propose to enumerate the empirical findings which are generally supposed to suggest the presence of organic pathology. Thirdly, it may be of interest to scan the methods which are now being developed to extend the scope of the subject.

The basic technical device which has been generally adopted is the employment of multi-channel direct recording instruments, with soundly planned bipolar electrode placements. The general acceptance of this technique is embodied in the recommendations drawn up in this country, in the United States and, more recently, by the International E.E.G. Committee.

In the early days of electro-encephalography, few centres used more than three channels of recording. Nowadays six is the preferred number; some centres use eight and one or two as many as twelve. It is generally agreed that the use of more than six recorders puts a great strain both on finance and on the interpretative ability of the recordist. For this reason a logical development has recently been introduced which can employ several score of channels without burdening the operator with yards of record. This device, which has been called a "Toposcope", exploits the fact that for certain purposes the information required about the patient is more a matter of topographic detail than of changes with respect to time. Accordingly, the electrical activity of the brain is displayed upon a cathode-ray oscilloscope of large diameter in such a way that the regions where electrical activity is in progress can be directly observed as a flickering light, giving the illusion that the observer is looking at the head of the patient and can see the significant discharges where they are actually occurring.

Another type of technical refinement is the automatic analysis of the records in terms of their various components, in the form of a frequency spectrum. This device is now fairly familiar. Its function is merely to assist the interpreter by disclosing components invisible to the naked eye and to provide quantitative information, where previously only qualitative descriptions were available. Automatic frequency analysis can be combined with toposcopy in such a way that the local activity of quite small cell groups can be detected and measured, and the anatomical dissemination or suppression of the various modes of activity can be quite accurately traced. This type of study is of particular value in organic conditions, as compared with, for example, cases of epilepsy, since there is less danger of overlooking transient or paroxysmal changes, which are still best studied by means of the conventional multi-channel recorder.

One of the most healthy signs in electro-encephalography is the tendency to include on the record a registration of other variables beside the E.E.G. itself, and thus, respiration, electrocardiogram, blood-pressure, skin resistance, muscular activity and so forth appear more and more frequently in electro-encephalographic tracings, so that the correlation of nervous and somatic perturbations can be more readily made.

The limitation imposed on ordinary electro-encephalography by having to record through the unopened skull is still serious. There is still no trustworthy method of distinguishing between cortical and basal activity, but the use of special electrode designs and placements has produced some promising results. The bipolar nasal or pharyngeal electrode provides at least a different approach to the basal structures, though these still remain relatively inaccessible to the electro-physiologist. When direct access can be obtained to the brain through a burr-hole or during an operation, both the cortex and the deeper structures can be explored with no more damage than is caused by the ordinary brain needle, which can be converted into a satisfactory bipolar electrode of small dimensions. Naturally, opportunities for such observations occur only in cases where organic disease is suspected, so that information on entirely normal human brains has not been obtained in this way, but in many cases the abnormal region occupies only part of the operative field so that direct comparisons of healthy and disturbed function can be made at all cerebral levels. Apart from the physiological interest of such data, the precise delimitation of subcortical new growth and abscess formations has been found of considerable practical value. This procedure, at least, requires only the simplest recording equipment and can be combined with the withdrawal of specimens for biopsy.

One may anticipate that valuable observations may be made in the future by combining the technique of direct exploration with the experimental procedures to be discussed later.

We may now turn to the enumeration of those features of the electro-encephalogram which are suggestive of organic pathology. It may be best to consider them, at first, quite empirically, in order to outline the scale of variation. First of all there are the classical slow rhythms which were originally called "delta" waves. A summary of the facts relating to these is contained in Table I. It will be seen that great care is necessary in interpreting records containing only this type of abnormal activity, particularly when the diagnosis lies between an organic condition and one of, for example, idiopathic epilepsy. The data summarized under the heading "Wave-form" are of the greatest importance, since it is the irregularity and variability of the discharges which seem to suggest an acquired lesion. It is tempting to suppose that this irregularity is due to the presence of many independent components, as suggested by the frequency analysis, for this would fit in well with the conception that the lesion

is producing a condition of what one might call "forced oscillation" on the part of the cell-groups near-by. One may, perhaps, consider this irregular polyrhythmic delta discharge as a strictly pathological phenomenon, at any rate when it is focal or limited in its extent. Its resemblance to the activity seen in deep sleep and in infants suggests a further speculation about the function, if any, of such slow rhythms. It is never satisfactory to regard a phenomenon as without significance and some years ago it was suggested that slow activity of this type may represent the activity of a mechanism whereby neurones are relieved of their normal function in disturbed conditions, thus taking the place in the brain which pain does in most other parts of the body. If this is really the function of slow activity in these conditions, one might expect that the imposition of slowly changing electrical currents on the brain from

TABLE I.—ABNORMAL E.E.G. FEATURES SUGGESTIVE OF ORGANIC PATHOLOGY

SLOW (delta, 0.5 to 3.5 c/s).

Amplitude: The larger the amplitude the greater the area involved.

Frequency: The lower the frequency the more acute and/or rapidly progressive the lesion. ("Sub-delta" 0.2 to 1 c/s characteristic of acute abscess.)

Wave-form: Irregular, polyrhythmic, non-harmonic (e.g. 1.5 + 2.5 c/s) near lesion. Monorhythmic, or harmonic in homologous area of opposite hemisphere or bilateral when lesion is deep.

Persistence: Persistent near lesion, paroxysmal and/or responsive in homologous or bilateral foci.

Topography: Diffuse resembles sleep and infancy, otherwise suggests raised intracranial pressure, toxic conditions. Focal good evidence of local pathology in all cases, but lesion often posterior to focus.

GENERAL SIGNIFICANCE

Cortical involvement when polyrhythmic and persistent.

outside might have a similar effect and I have personally experienced that this is, in fact, the case; when a current of about 20 milliamps fluctuating at one or two cycles per second is passed through the head by means of electrodes of the conventional E.E.G. type, a drowsy and inattentive state of mind can be induced. These experiments are still incomplete but it would certainly be a relief to assign a specific function to the slow activity, so useful to the electro-encephalographer. It is worth noting, also, that as well as delta activity from the neighbourhood of a region of a cortical lesion, more rhythmic delta waves are often seen from remote regions; this type of disturbance often resembles the normal spontaneous rhythms in being responsive to physiological stimulation, and seems to follow the normal anatomical pathways. For this reason it has been called "quasi-physiological" and it often gives a most valuable clue to the extent of the lesion itself: sometimes, at least, it is associated with recent interference with certain anatomical circuits and commissures.

Table II shows some abnormal appearances which are classed under theta activity. This sobriquet was originally given to rhythms found in cases of subcortical tumour but the term has since been adopted quite legitimately to include, also, rhythms in the same frequency band which are associated with functional, rather than organic, disorders. It is interesting that the identity of this type of rhythm was not recognized until the advent of automatic analysis; until then it was usually referred to as a "slow alpha rhythm" but its significance is quite different from that of the various aberrations of alpha activity, to be described later. Records containing theta activity are much harder to interpret than those with the classical delta rhythm and there is only very rarely a truly focal theta discharge. Perhaps the most trustworthy pathological sign is a persistent inalterable rhythm in the theta band and this is more satisfactory when it is unilateral. It is almost impossible to be certain of pathology when theta rhythm is encountered in children below the ages of 10-12, if only a single record is taken. Here again, persistence is an important diagnostic feature, since the theta components of children's records are characteristically labile, both in terms of

Another type of technical refinement is the automatic analysis of the records in terms of their various components, in the form of a frequency spectrum. This device is now fairly familiar. Its function is merely to assist the interpreter by disclosing components invisible to the naked eye and to provide quantitative information, where previously only qualitative descriptions were available. Automatic frequency analysis can be combined with topography in such a way that the local activity of quite small cell groups can be detected and measured, and the anatomical dissemination or suppression of the various modes of activity can be quite accurately traced. This type of study is of particular value in organic conditions, as compared with, for example, cases of epilepsy, since there is less danger of overlooking transient or paroxysmal changes, which are still best studied by means of the conventional multi-channel recorder.

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engage the activity of several fundamental physiological mechanisms, yet is a most ominous sign. It is most common in young people and is always associated with a history of some sort of seizure, though there is not always evidence that the patient is having an attack while this discharge is in progress. It has recently been observed that discharges of this type can often be evoked or driven by physiological stimuli, when these are presented at a frequency near to that of the spontaneous discharge rate. Occasionally even non-rhythmic stimulation can precipitate or accentuate this discharge.

This leads on to the sixth class of abnormal features, the anomalies which can be observed in the electrical responses evoked by various types of stimuli. Photoc stimulation is the most convenient and effective form of stimulus, if for no other reason because the areas concerned with vision and visual association are so large and accessible in man. In normal subjects the type, degree and extent of the response are very variable both from person to person and from moment to moment. Here again, the degree of symmetry is an important factor, though, even in this respect, certain normal persons present a startling picture. Of course when there is widespread destruction of the visual areas no response can be evoked from that region, but rather harder to understand is the tendency of areas adjacent to damaged or dys-

ABNORMAL E.E.G. FEATURES SUGGESTIVE OF ORGANIC PATHOLOGY

TABLE II.

THETA (4 to 7 c/s).

Amplitude: Greater than 20 μ V in adults but resembles psychopathy.

Frequency: Typically 5 to 6 c/s.

Wave-form: Simple.

Persistence: Persistent when deep structures directly involved. When paroxysmal or responsive (to physical or emotional stimuli) resembles psychopathy and juveniles.

Topography: When focal suggests underlying deep lesion. When diffuse wide involvement of deeper structures (trauma, tumour).

GENERAL SIGNIFICANCE

Involvement of cortico-thalamo-hypothalamic circuits and structures near third ventricle.

TABLE III.

ALPHA (8 to 13 c/s).

Asymmetry

(a) *Amplitude:* Greater than 50% between hemispheres.

(b) *Topography:* Extension beyond parieto-occipital region. Restriction to less than 50% area on normal side.

Asynchrony

(a) *Frequency:* Consistently more than 0.5 c/s between hemispheres.

(b) *Fluctuation:* Frequent unilateral bursts.

Persistence: Total persistence (resembles certain psychotic conditions).

Asymmetrical Responsiveness: To either mental or physical stimuli beyond known normal limits.

TABLE IV.

SPIKES

Usually focal, sometimes bilateral.

GENERAL SIGNIFICANCE

Cortical irritation; usually associated with seizures. Frequently result of trauma, particularly birth trauma.

SLOW SPIKE AND WAVE (*not* wave and spike of *petit mal*)

Often focal but sometimes bilateral. Most common in children.

GENERAL SIGNIFICANCE

Profound pathology of varied and unknown types, associated with minor, akinetic and myoclonic seizures.

EVOKED ACTIVITY (Photoc Stimulation)

Absence of response at fundamental stimulation frequency. Disproportionately large response at harmonic frequencies above 18 c/s.

trophic projection fields to exhibit activity only at frequencies harmonically related to that of the stimulus rate. It would appear as though in such cases the response to

minutes and months. This is an opportune stage to emphasize the enormous importance of repeated recordings in cases of suspected organic disease. The French workers have devoted much attention to what they call the anatomo-clinical evolution of the E.E.G. and all workers would agree that the changes in the picture from day to day or week to week are of great importance, both in distinguishing organic from functional and epileptic disorders and in helping to establish a differential diagnosis as between static, recovering and progressive lesions. While considering the question of theta rhythms it should be emphasized that these components are not simply a milder form of delta activity; they do not occur merely as a result of slight cortical damage but are definitely correlated with a subcortical disturbance and particularly with perturbation of the relations between the cortex and basal structures. Moreover, the occurrence of rhythms in this frequency band in normal people, in certain transitory, emotional states suggests that they may have a function analogous to that of the better-known alpha rhythm in subserving the mechanism of sensorimotor integration.

The relation between the amplitude and extent of delta and theta activity, both topographically and temporally, can be used to infer the extent and rapidity of evolution or decline of a pathological process. For example, cases in which the first abnormal feature is a diffuse but lateralized theta discharge followed after a matter of weeks or months by a more focal delta rhythm on the same side have been found post mortem to have tumours arising near the third ventricle and growing outwards. An inverse relationship in order of time suggests a lesion arising superficially, invading the deeper structures. There are, however, many anomalies and paradoxes in such cases and, as always, these often provide evidence of important fundamental truths.

Table III indicates, briefly, some of the disturbances in the normal alpha rhythms which can be taken as abnormal signs. Clearly, when an area of the brain, normally associated with alpha activity, is destroyed, the rhythm is absent from that region and the same is, of course, true of the smaller, less rhythmic components of the E.E.G. There are, however, cases more complex than this; the interpretation of such records depends largely upon comparison of the two hemispheres, since the normal variations of symmetry are very much less than those of alpha activity as a whole. There are normal people who show no alpha activity whatever and those in whom the rhythm can be blocked only by the reading aloud of an interesting sentence. Rather as in the case of the theta rhythm, abnormalities in the alpha category are more often signs of interference with physiological circuits and anatomical pathways than of cortical involvement, and for this reason such cases should be studied by experimental methods in order to work out the site and nature of the interference. Here again also, automatic analysis is a great help not only in separating the various components but also in identifying their focus and extent, a very difficult task when several rhythms of similar frequency are spatially adjacent or overlapping.

Table IV contains several other abnormal features. The brief discharges generally called "spikes" are as truly abnormal as the focal delta discharge but have, of course, an entirely different significance. They are almost certainly signs of irritation rather than depression and are usually very localized when they occur in relation to trauma. As the Montreal School has demonstrated, they often arise a little distance away from the apparently traumatized area and indicate a target for intervention even better than do the obvious signs of damage.

A very peculiar and still poorly understood feature in certain records is the slow spike-and-wave complex which, in some ways, resembles but is actually quite distinct from the classical wave-and-spike discharge associated with minor seizures. This is actually one of the most intriguing of all cerebral abnormalities since it appears to

syphilis or disseminated sclerosis, and to Dr. D. L. Davies for a group of 14 cases of Friedreich's ataxia which he has studied and which I have included here.

Table I shows the diagnostic groupings studied. It is seen that the E.E.G. is abnormal in 45% of the total group, but tends to be more abnormal in the inflammatory than in the degenerative cases and particularly severely in the G.P.I.s, the presenile cortical atrophies and in Huntington's chorea. It is rarely abnormal in disseminated sclerosis. Of the cases with severely abnormal E.E.G.s (16 in number), 4 are acute cases of G.P.I. and 4 cases of presenile atrophy with gross mental confusion or fits. There is a case of Friedreich's ataxia with episodes of automatic behaviour considered epileptic, a case of Wilson's disease, 2 recent severe vascular accidents and the remaining 4 cases showed mental confusion.

TABLE I.—E.E.G. IN ORGANIC CEREBRAL DISEASE
(Excluding Neoplasm and Trauma)

	No. of cases	E.E.G. abnormal	E.E.G. severely abnormal
<i>Inflammatory (46)</i>			
G.P.I.	16	9	4
Other neurosyphilis	14	1	0
Post-encephalitic	16	13	0
<i>Degenerative (89)</i>			
Presenile cortical atrophy	16	8	4
Friedreich's ataxia	14	3	1
Huntington's chorea	6	5	5(?)
Cerebro-cerebellar degeneration	12	4	1
Vascular accidents	12	5	2
Cerebral arteriosclerosis	5	2	1
Prolonged cerebral anoxia	4	3	1
Disseminated sclerosis	13	2	0
Chronic drug intoxications	5	4	1
Malignant hypertension	2	2	1
<i>Others (9)</i>			
P.M.A. Sturge-Weber's syndrome, compulsive tic, arteriovenous aneurysm, sup. long. sinus syndrome, congenital alexia, essential hypertension	9	4	0
Total	144	65	16 (? 21)

Note: If the five patients with Huntington's chorea and absence of rhythmical activity are included there are 21 severely abnormal E.E.G.s (see text).

TABLE II.—SYMPTOM GROUPS

	No. of cases	E.E.G. correlation	E.E.G. severely abnormal
Aphasia	10	—	—
Retinal blindness	5	—	—
Chronic hemiplegia	14	—	—
Cerebellar ataxia	21	—	—
Parkinsonism	8	—	—
Parkinsonism + behaviour disorder	8	+	—
Choreo-athetosis	6	—	—
Gross mental confusion	5	+++	+
Intellectual deterioration	29	+	—
Fits	16	+	—

I have attempted a further analysis from 122 relevant cases between the *main symptom groups* (Table II), the involvement of *special systems* within the C.N.S. and the E.E.G. findings. Finally, the abnormal E.E.G. patterns themselves have been examined and four types have emerged with considerable frequency (Table III). These

the stimulus was arriving by an indirect route at the secondary areas and filtered by some intervening mechanism, so as to contain only the higher components of the primary response. There is a peculiar biochemical relationship in some of these cases; a lowered blood sugar enhances the effect, which may be almost negligible after a heavy meal or when glucose has been drunk. This, again, suggests that elementary physiological mechanisms are revealed and of these, so far, we know almost nothing.

Consideration of this summary of facts and notions leads one to the conclusion that future progress in applied electrophysiology will depend more and more upon intimate knowledge of the functional anatomy of the nervous system and rather less upon technical contrivances. The line of approach taken by Dusser de Barenne and continued so ably by his pupils and collaborators has brought many of the bewildering diagrams in the anatomical textbooks to life and discoveries in this field are reported almost daily. There is no doubt that within a few years it will be possible to rely upon a complete functional anatomy of the central nervous system and this very great victory will be reflected in the value and scope of electro-encephalography.

Side by side with this advance goes the study of the subtle and elusive mechanisms of central nervous action. It is peculiar that we have dallied so long with the electrical phenomena represented in the electro-encephalogram, without insisting upon their identifying themselves in relation to function. The modern concept that the spontaneous rhythms seen in the brain may have a specific and essential part to play in transforming sensory data into material for conscious perception helps considerably to explain some of the aberrations and anomalies listed above.

It is, perhaps, inevitable that, being a physiologist, I should seem to consider the desperate human problems presented by organic cerebral disorder more as preparations than as patients. It is one of the great pleasures of this work that at all times this cool and detached attitude can be moulded and orientated by the enthusiastic collaboration of the physicians and surgeons who have humanitarian, as well as scientific, duties.

Dr. Denis Hill: The value of electro-encephalography as a clinical test for the location of space-occupying lesions of the cortex and subcortical centres is now generally recognized. There is an extensive literature and recent reviews have compared the technique favourably with other clinical methods and with the use of air-replacement. The position regarding trauma of the brain is similar, although it has received less attention. A few reports have appeared of the E.E.G. findings in acute and chronic encephalitis and in neurosyphilis, but none, as yet from this country. In the case of expanding lesions and cerebral trauma, the extent of the damage to nerve tissue is usually widespread, is not confined to any specific pathways or systems and the effects upon the E.E.G. are often the result of widespread destruction, cerebral œdema or raised pressure in the ventricles. It is only rarely in the case of the expanding lesion that the changes in the E.E.G. can be related to impairment of function within known functional pathways. Consideration of the chronic degenerative processes in which the sites of pathological lesions are known might provide evidence of the relation between such lesions and particular changes in the E.E.G. My remarks will, therefore, be concerned with the findings in 144 cases of organic disease of the nervous system, a group collected from the material at the National and Maudsley Hospitals, to exclude expanding lesions. The group includes 46 inflammatory cases and 89 cases classed as degenerative. Since patients with such conditions are not usually referred for E.E.G. examination, the number is not large considering that it represents the total collected over a period of four years. I am indebted to Dr. Worster-Drought who referred from the West End Hospital 25 patients with neuro-

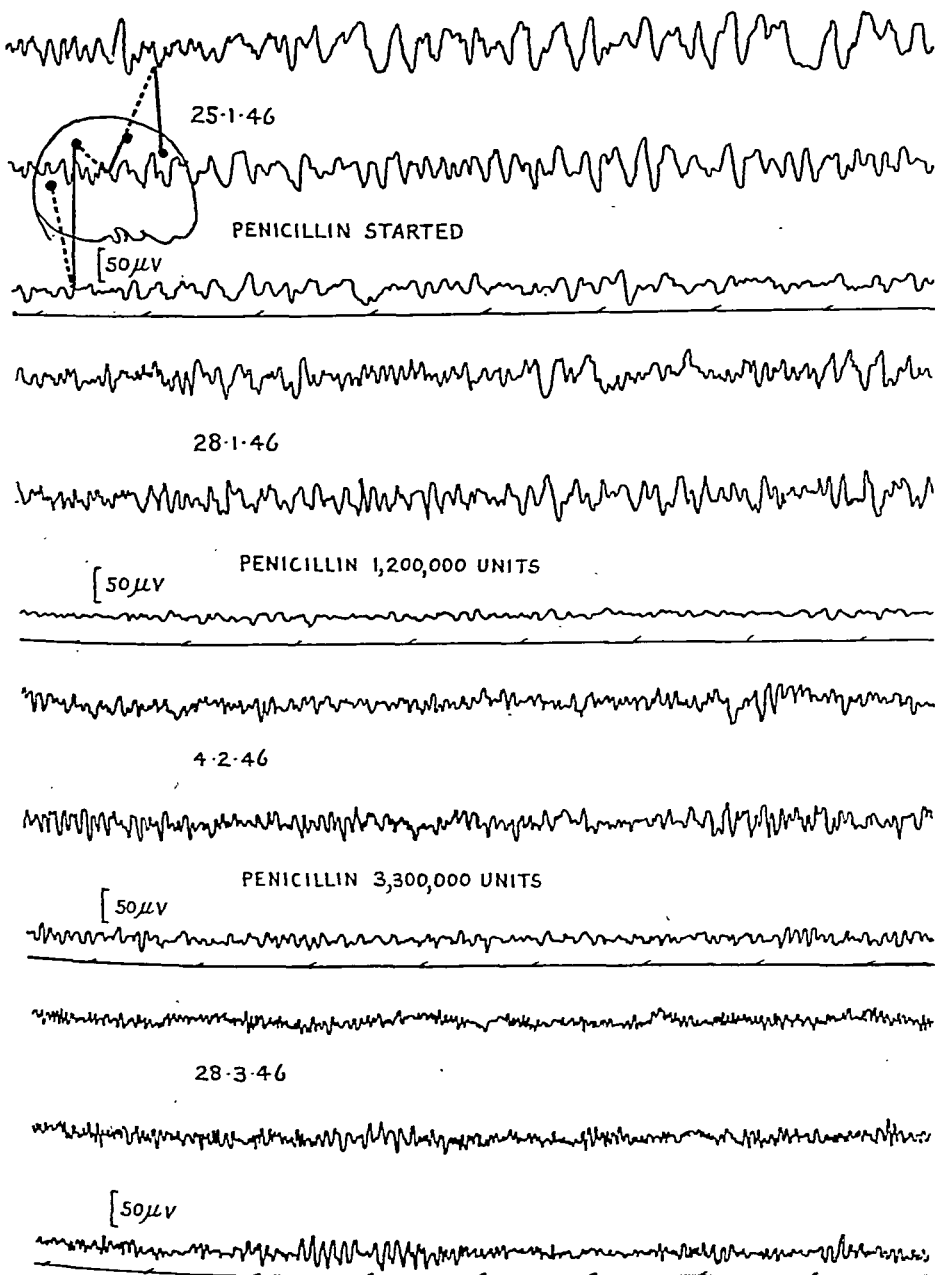


FIG. 1.—Treatment of patient with G.P.I. by penicillin. 25.1.46. (before treatment started): High voltage generalized 3-4 c/sec. delta rhythm, maximal in frontal areas; patient disoriented with gross mental confusion. 28.1.46: Marked reduction in delta rhythm; emergence of occipital "slowed alpha" rhythm at 6-8 c/sec., and frontal fast rhythm. 4.2.46: Further improvement; no delta rhythm. 28.3.46: Normal occipital alpha rhythm at 9-10 c/sec. Generalized fast rhythm. Sensorium clear but failure of memory for recent events.

four types have been related to the presumed sites of action of the lesion present. The clinical data on which this has been done was necessarily not always complete.

INVOLVEMENT OF SPECIAL SYSTEMS

Degeneration in the large afferent and efferent systems in the spinal cord, seen in the cases of Friedreich's ataxia and tabes dorsalis, did not influence the E.E.G. Cases of cerebellar agenesis and degeneration were also normal. 2 cases of oculomotor nuclei degeneration were normal. 5 cases of choreo-athetosis were normal but a case of Wilson's disease was severely abnormal. Marked changes were found in 5 out of 6 cases of Huntington's chorea, but none in post-encephalitic Parkinsonism, without severe personality changes. In view of the known importance of thalamic nuclei for the production of cortical rhythms it is unfortunate that no patient has been examined in whom the predominant lesion could be ascribed to the thalamus. Turning to the predominantly cortical lesions, whether the E.E.G. is abnormal would appear to depend on the acuteness and severity of the lesion. Unilateral vascular lesions, embolic or thrombotic, leave the E.E.G. abnormal on the side for a few days or weeks, but later the rhythms tend to return to normal. In presenile atrophy also, during the acute phases of the condition, the E.E.G. is very frequently abnormal and often focal, but later may become normal again. The case of G.P.I. is very similar and 5 treated patients within this series had normal E.E.G.s. (Fig. 1) In a number, however, this was not the case and it would seem that the appearance of a new pattern of E.E.G. rhythm supervening after an acute inflammatory or degenerative process tends to conform to a type and to be associated with diffuse cortical destruction and with some degree of intellectual deterioration.

TYPES OF E.E.G. ABNORMALITY

The types of E.E.G. abnormality found can be classified under four headings:

- (1) Generalized delta rhythm (less than 4 c/sec.) which is rhythmical and symmetrical in the frontal areas. Local delta rhythm, which is usually irregular, containing poly-rhythmic components.
- (2) Theta rhythm excess (4-7 c/sec.) bilateral, parieto-temporal and symmetrical.
- (3) "Slowed" atypical alpha rhythm 6-8 c/sec. occupying the post-central areas, showing poor blocking response to visual attention.
- (4) Absence of rhythmical activity, in all areas or in a local area, at rest, on eye closure and during overbreathing.

TABLE III

Type	Clinical groups	Symptom correlates
(1) (a) Generalized delta (<4 c/sec.)	(a) Acute G.P.I. Acute vascular accidents Drug or hypertensive encephalopathy	Mental confusion
(b) Local delta	(b) Acute vascular accidents Acute G.P.I. Acute cortical atrophy (presenile)	Fits
(2) Theta rhythm excess (4-7 c/sec.)	General: Especially post-encephalitic	Behaviour disorder Personality change
(3) "Slowed alpha" (6-8 c/sec.)	Chronic diffuse cortical inflammatory and degenerative processes	Dementia
(4) Absence of rhythmical activity		
(a) General	(a) Huntington's chorea	
(b) Local	(b) Severe local atrophic lesions in chronic stage	

by mechanical and chemical stimulation of local cortical areas, particularly in the frontal regions, but this mechanism is purely cortical and does not involve subcortical "suppressor" circuits.

In the light of these physiological observations it is of interest that cortical rhythms are unaffected by the lesions of choreo-athetosis but suppressed by those of Hunting-

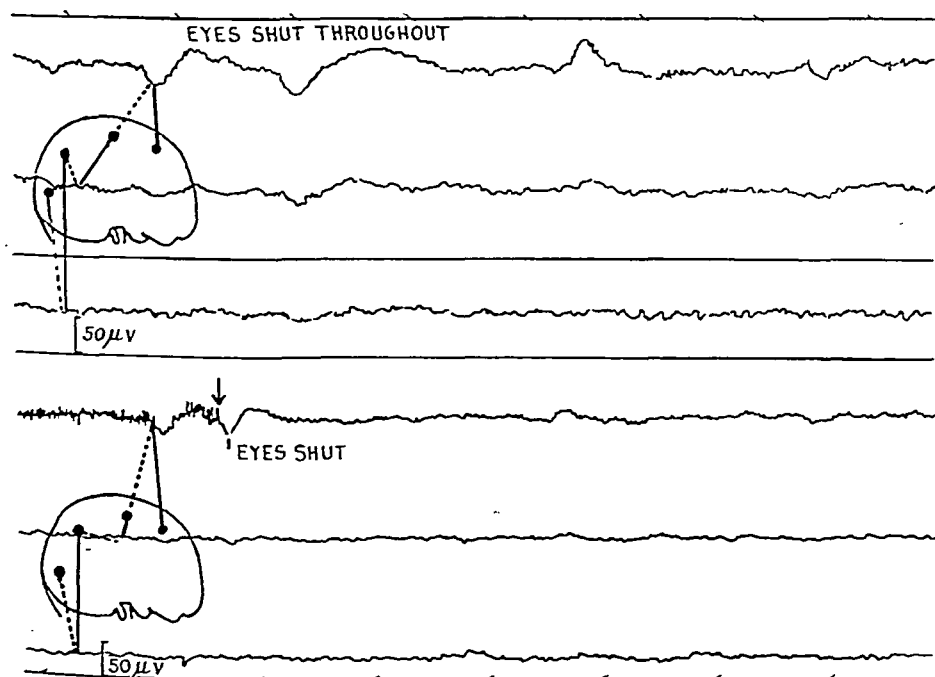


FIG. 3.—Two cases of Huntington's chorea. Absence of rhythmical activity with the eyes shut. No change during or after voluntary overbreathing.

ton's chorea. It seems improbable that deterioration within the thalamic nuclei could have been sufficient to account for the absence of rhythmical activity in 5 out of 6 cases, nor is it likely that the posterior hypothalamic nuclei were destroyed in these cases. It is probable that the association of an atrophic process in the frontal cortex and in the basal ganglia is the significant factor since neither alone produces either persistent depression or facilitation of cortical rhythm.

To summarize, the normal rhythmical activity of the postcentral cortex, called the alpha rhythm, is dependent upon intact cortical neurones, especially the deeper layers, and upon thalamo-cortical connexions. From the present series of cases, nothing can be learnt about the effects of lesions within the thalamus. When large areas of cortex are *destroyed*, the areas involved may show little rhythmical activity, a state similar to a local "suppression" described by Dr. Denis Williams (1945). When the cells of large areas of cortex are involved in *dysfunction* from toxic, inflammatory or degenerative processes, local very slow or delta wave activity occurs. Whether the E.E.G. in the area returns to normal or shows absence of activity later would appear to depend upon the degree of recovery and the extent of the final cellular destruction. If epileptic activity supervenes in the cortex near-by an area of destruction, a persistent E.E.G. abnormality may remain of epileptic type. Interference with thalamo-cortical projections on one side results in diminished rhythmical activity on that side.

10 cases of "slowed" alpha rhythm occurred. These were 5 cases of presenile dementia, one post-encephalitic state, 3 patients with diffuse vascular disease (fig. 2, one case illustrated) and one patient with Gilles de la Tourette syndrome.

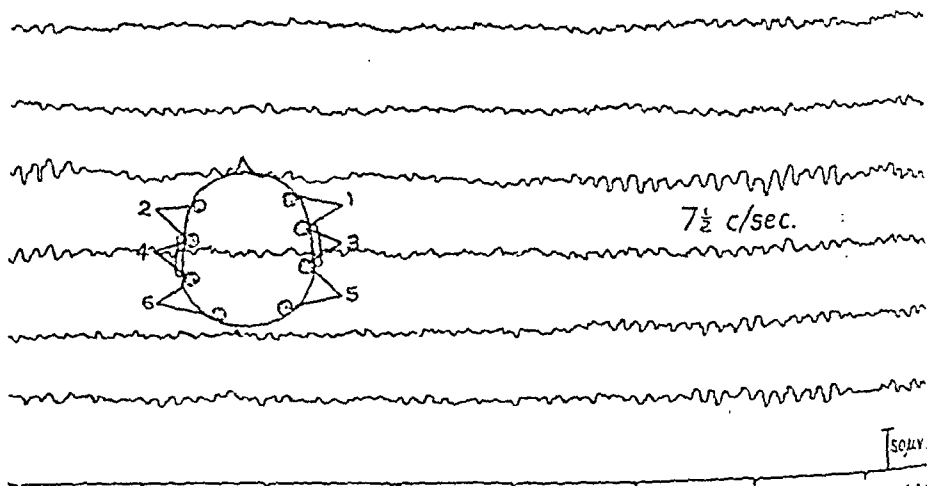


FIG. 2.—Cerebral vascular disease; aphasia. "Slowed alpha" rhythm at $7\frac{1}{2}$ c/sec. Slight reduction in the amplitude of activity in the anterior parts of the lead on the left side.

DISCUSSION

I believe that this is the first report of the E.E.G. findings in Huntington's chorea, choreo-athetosis, Friedreich's ataxia and other cerebellar degenerations. Recently interest for electro-encephalographers has shifted from the cerebral cortex to the thalamus and basal ganglia, clinically because of Dr. Grey Walter's finding of theta rhythm excess in cases of tumours around the third ventricle, and physiologically because of the effects on cortical rhythms of ablation and stimulation of subcortical grey matter, reported by Kennard and Nims (1942), Morison and Dempsey (1943), Murphy and Gellhorn (1945), Obrador and others (1943). The finding of a "suppression" or absence of cortical rhythm in cases of Huntington's chorea (fig. 3), in which both basal ganglia and cortex suffer degeneration, must be contrasted with cases of choreo-athetosis and Parkinsonism in which the E.E.G. is normal and with cases of post-encephalitic Parkinsonism with severe personality and mental changes in which an excess of theta rhythm is found.

Experimental work on animals has shown that both these effects—the facilitation of slow activity and the "suppression" or abolition of all cortical activity—can be produced by interference with subcortical grey matter. Thus, stimulation of the striatum by Gerebtzoff (1941) produced abolition of cortical rhythms, while destruction produced an excess of theta rhythm. Murphy and Gellhorn found that electrical stimulation of the posterior nuclei of the hypothalamus produced fast rhythms in the cortex while Obrador (1943) found that destruction in this area resulted in abolition of the normal potentials.

The common path for both these effects on the cortex must be through thalamic nuclei:—In the case of the striatum via globus pallidus and possibly lateral ventral thalamus, in the case of the hypothalamus via mammillothalamic tract and dorso-medial nucleus. In the case of the hypothalamic-thalamic system it has been shown that the areas of the cortex which will fire the hypothalamus lie in the prefrontal, sensorimotor and cingulate gyri. It has also been shown (Leao and Morison 1945) that spreading depression of cortical activity over both hemispheres can be induced

by mechanical and chemical stimulation of local cortical areas, particularly in the frontal regions, but this mechanism is purely cortical and does not involve subcortical "suppressor" circuits.

In the light of these physiological observations it is of interest that cortical rhythms are unaffected by the lesions of choreo-athetosis but suppressed by those of Hunting-

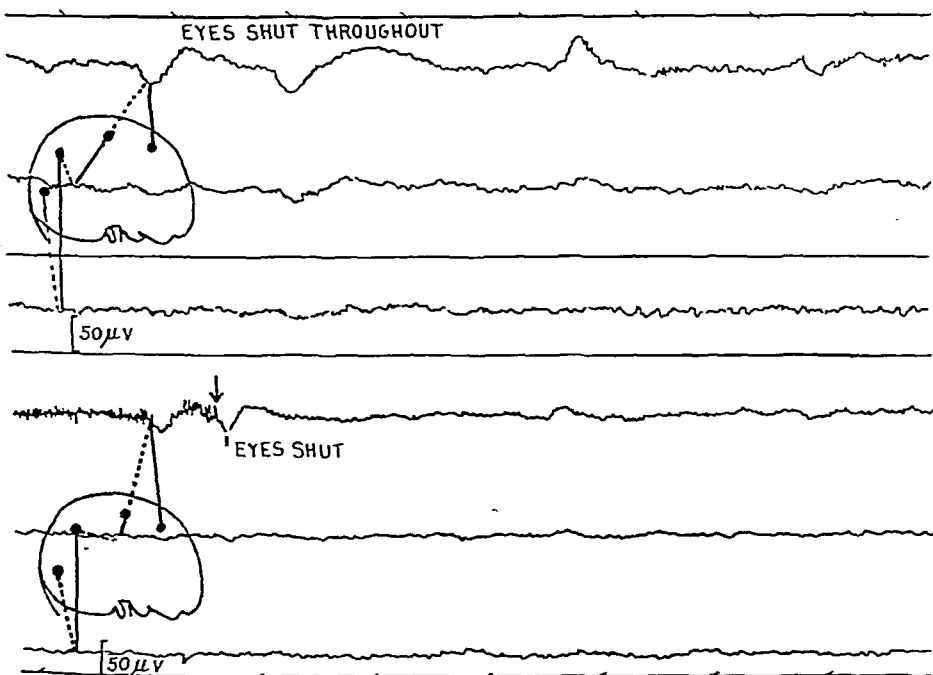


Fig. 3.—Two cases of Huntington's chorea. Absence of rhythmical activity with the eyes shut. No change during or after voluntary overbreathing.

ton's chorea. It seems improbable that deterioration within the thalamic nuclei could have been sufficient to account for the absence of rhythmical activity in 5 out of 6 cases, nor is it likely that the posterior hypothalamic nuclei were destroyed in these cases. It is probable that the association of an atrophic process in the frontal cortex and in the basal ganglia is the significant factor since neither alone produces either persistent depression or facilitation of cortical rhythm.

To summarize, the normal rhythmical activity of the postcentral cortex, called the alpha rhythm, is dependent upon intact cortical neurones, especially the deeper layers, and upon thalamo-cortical connexions. From the present series of cases, nothing can be learnt about the effects of lesions within the thalamus. When large areas of cortex are *destroyed*, the areas involved may show little rhythmical activity, a state similar to a local "suppression" described by Dr. Denis Williams (1945). When the cells of large areas of cortex are involved in *dysfunction* from toxic, inflammatory or degenerative processes, local very slow or delta wave activity occurs. Whether the E.E.G. in the area returns to normal or shows absence of activity later would appear to depend upon the degree of recovery and the extent of the final cellular destruction. If epileptic activity supervenes in the cortex near-by an area of destruction, a persistent E.E.G. abnormality may remain of epileptic type. Interference with thalamo-cortical projections on one side results in diminished rhythmical activity on that side.

The E.E.G. can also be altered by lesions in some fibre systems terminating in the thalamus, but is unaffected in cerebellar lesions, mid-brain lesions or lesions of the long sensory tracts. Lesions confined to the extrapyramidal system do not alter the pattern, which is normal in choreo-athetosis and Parkinsonism. How the depression of cortical activity in Huntington's chorea is mediated remains an interesting problem.

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Dr. Denis Williams: *The clinical use of the electro-encephalogram.*—Many papers have been written about the use of the electro-encephalogram (E.E.G.) in the localization of cerebral lesions, and there has generally been a reasonable correlation between the predicted and actual site of the lesion. In any study of these contributions there is a natural tendency to link the E.E.G. changes to the causal lesion, and to forget that the electrical abnormalities which are seen arise, in fact, from the brain which is damaged by the lesion.

Dr. Grey Walter has given us an outline of the recent advances in electro-encephalographic technique and of their applications to the interpretation of the different wave-forms seen in the abnormal E.E.G. He has also related some of the groups of abnormal rhythms to the groups of clinical disorders which are mainly responsible for them. Dr. Denis Hill has analysed the contributing causes of abnormalities in the E.E.G. in some of the conditions which are associated with an impairment of consciousness. I would like to consider briefly the part the E.E.G. has to play in contributing to knowledge about the nature of lesions in the cerebral hemispheres, quite apart from its admitted value in localizing them.

No single clinical method can be used, alone, to establish a complete understanding of the kind of lesion which might be present in any organ, but the clinician finds it necessary to integrate all the evidence he can accumulate to hazard a reasonable prediction of the characteristics of an unseen lesion which is causing a demonstrable disorder. Similarly the E.E.G. cannot often be used, alone, to establish a diagnosis. It must be related to all other clinical, pathological, and radiological data which have been placed at his disposal.

What further information can the E.E.G. give about the nature of a lesion of the hemispheres, apart from its approximate site? It seems that it may give evidence upon six of its qualities.

(1) *Extent.*—The E.E.G. merely records the electrical activity of damaged brain tissue, but the area of this can be mapped out within the limitations of a technique which includes recording through the thickness of the scalp and cranium. Disordered brain may for instance be found in the other hemisphere, or even in the unexpected hemisphere. The sharpness of definition of the abnormality may also be judged.

(2) *Severity.*—The degree of damage which is taking place at the time of recording may be judged by the period, voltage and persistence of the abnormal waves. Complete destruction may go unobserved, or may be recognized in abolition of the normal rhythms.

(3) *Absolute destruction* may be recognized by a "silent area" in which there is absence or reduction of electrical activity, but its certain recognition must often wait upon relating the E.E.G. and the radiological changes.

(4) *The depth* of the lesion in the hemispheres may be surmised, at least to a consideration of whether it lies in the cortex, the white matter, or the basal ganglia, by relating clinical observations to the voltage and period of the abnormal waves, and to the extent of their diffusion over the scalp. For instance, low voltage 3-a-second waves, obtained over a wide area in one hemisphere, particularly if associated with 7-a-second waves in one or both hemispheres, suggest a deep lesion.

(5) *Secondary changes*.—Long-standing lesions give rise to characteristic changes in the E.E.G. which have many features by which they can be distinguished from the immediate and direct effects of brain damage on the E.E.G. These secondary changes often precede, or are associated with, epilepsy.

(6) *Associated changes*.—Physical disorders which may be associated with cerebral lesions give widespread changes in the E.E.G. which are often symmetrical, and fairly easily recognized. Such changes are seen with high intracranial pressure, changes in consciousness, or in toxic states. For their correct interpretation knowledge of the clinical story is essential.

It is clear that in each of these six instances the E.E.G. can only be interpreted reasonably if the interpreter has full knowledge of other aspects of the clinical problem. That this is essential is made evident by the fact that there is usually more than one—and there may be many—possible explanations for any isolated phenomenon which may occur in the E.E.G. Even a sequence of related phenomena in the E.E.G. may be unsusceptible of interpretation if considered alone. For example:

(1) With a suspected lesion of the hemisphere, absence of abnormal slow waves in the E.E.G. may be due to absence of any lesion or to complete destruction of the damaged brain. For example, a large meningioma or a large porencephalic cyst may be associated with normal E.E.G. records.

(2) Suppression of normal rhythms in both hemispheres may be due to widespread destruction of parenchyma, to recent and benign concussion, or to personal idiosyncrasy.

(3) Episodes of abnormally fast waves may recur in widely dissimilar conditions, such as epilepsy, syncope, intoxications with drugs, such as medinal, or again as a personal idiosyncrasy of a normal subject.

(4) Episodes of slow waves are seen in epilepsy, in states of impaired consciousness, in normal sleep, and also in association with psychopathy.

There are even circumstances in which it is quite impossible to recognize which is the abnormal hemisphere, when unilateral changes are seen in the E.E.G., unless clinical data are available. When, however, the clinical findings are related to the E.E.G., further information is immediately available upon the nature of the lesion. For instance, abnormal rhythms recorded from the right side of the scalp in a patient with a right hemiplegia and aphasia suggest that the absence of abnormality from the left and presumably abnormal hemisphere is due to suppression of activity here. This suppression, with no abnormal slow waves, indicates that at the time of recording the left-sided lesion is causing no active brain destruction. Such a state of affairs is found with benign tumours, or after vascular catastrophes. The clinical story will probably distinguish between these two conditions. Such a record would eliminate, for instance, a malignant glioma, a secondary carcinoma, or a recent abscess.

Even when the E.E.G. is found to be perfectly normal, a clinical story may be essential for a correct interpretation. Conditions in which this may be so are as follows:

(1) When several symptoms and signs persist after a head injury. If the E.E.G. has returned to normal no further organic resolution can occur, and the prognosis for functional recovery is correspondingly bad. This is so whether the disorder is the result of brain destruction or of associated neurotic illness. So long as abnormality is still present in the E.E.G. and resolution is still occurring a final bad prognosis need not necessarily be made.

(2) When a normal E.E.G. is found in an epileptic the story must be known, for it may be a chance finding in a severe constitutional epileptic or it may be used to support the tentative diagnosis of cysticercosis, since the E.E.G. is normal as often in this condition as in the normal population.

(3) When organic dementia is taking place as a result of a slowly progressive condition such as cerebral arteriosclerosis or Alzheimer's disease, the E.E.G. is usually normal. Here again, therefore, when the clinical story is known the normal E.E.G. should be used to approach a correct diagnosis and a reasonable prognosis.

(4) If a normal E.E.G. is found in a patient who on other grounds is thought to have an expanding lesion of the hemispheres, the differential diagnosis is much reduced, since the more malignant and actively infiltrating tumours are improbable, and a recent abscess impossible.

From the argument which has been advanced in this short paper it seems that the E.E.G. should not be used alone to localize a cerebral lesion. It should rather be interpreted with the help of all the other evidence, which may have been quite sufficient to localize the lesion, to add to the knowledge of the site, extent, and severity of brain damage occurring at the time, and also to reveal the other associated, and perhaps unexpected, changes which may be taking place.

Records and case abstracts were then given to show the way in which the E.E.G. has been used recently to elucidate changes, and clinical changes to elucidate obscure E.E.G. findings.

ERRATUM

Section of Neurology, Vol. 41, February Number, page 96, fifth line from bottom, for "Dr. R. N. Herson's case (*Lancet*, 1947 (ii), 491)" read "Dr. R. N. Herson's case (*Brit. med. J.*, 1947 (ii), 491)".

Section of Physical Medicine

President—W. S. TEGNER, M.R.C.P.

[January 14, 1948]

Surgery in the Treatment of Rheumatoid Arthritis and Ankylosing Spondylitis

By W. ALEXANDER LAW, O.B.E., M.D., F.R.C.S.

ABSTRACT.—The pain, deformities and disabilities resulting from rheumatoid arthritis and ankylosing spondylitis must be treated by a team composed of physician, physical medicine expert, orthopaedic surgeon, and, in certain cases, deep X-ray therapist working simultaneously.

The principle of "rest" in order to relieve pain has to be combined with methods designed to preserve and restore function. The multiple joint deformities in these cases may necessitate a long programme of reconstructive or functional treatment, which entails whole-hearted co-operation on the part of the patient in intensive post-operative exercise regime.

Procedures advocated for the upper limb include excision of the acromion process together with the subacromial bursa to allow free movement between the central tendon of the deltoid and the tendinous shoulder cuff: arthrodesis of the shoulder in cases where there is more severe joint destruction; in certain cases of elbow-joint arthritis, excision of the radial head and sub-total synovectomy may preserve joint function and avoid or delay the necessity for arthroplasty which can be carried out in two ways: (a) similar to the formal joint excision, or (b) re-shaping the lower end of the humerus and upper end of the ulna lining these surfaces with fascia. The former method is preferable in cases of rheumatoid arthritis. To overcome wrist-joint deformity and restore pronation and supination excision of the lower end of the ulna together with radiocarpal fusion in position for optimum function is advocated. Finger and toe joints may be corrected by resection of the bone ends and capsulectomy.

In the lower limbs bilateral involvement of the hip-joint is best treated by vitallium mould arthroplasty which may be carried out in four ways: (1) Routine arthroplasty; (2) Modified Whitman procedure; (3) Modified Colonna operation; and (4) The proximal shaft or intertrochanteric arthroplasty. It is essential in these operations to have knowledge of the operative technique, the use of special hip gouges and reamers, and detailed post-operative supervision.

For dorsal kyphosis of the spine, spinal osteotomy at the lumbar level provides excellent correction but is an operation demanding care and skill in its execution.

The author's remarks are based on experience gained when working with Dr. M. N. Smith-Petersen at the Massachusetts General Hospital, Boston, U.S.A.

RÉSUMÉ.—Le traitement de la douleur, des déformités et de l'infirmité qui résultent de l'arthrite rhumatoïdale et de la spondylite ankylosante nécessite le travail simultané d'une équipe composée du médecin, de l'expert en médecine physique, du chirurgien orthopédiste et, dans certains cas, du thérapeute pour la radiothérapie profonde.

Le principe du "repos" pour le soulagement de la douleur doit être combiné avec les méthodes destinées à préserver ou à rendre la fonction.

Les déformités articulaires multiples dans ces cas peuvent rendre nécessaire un long programme de traitement reconstructif ou fonctionnel, demandant la coopération absolue du malade dans un régime d'exercices postopératoires intensifs.

Les procédés recommandés pour le membre supérieur comprennent l'excision du procès acromial avec la bourse sous-acromiale, pour permettre le mouvement libre entre le tendon central du muscle deltoïde et la manchette tendineuse de l'épaule; l'arthrodesis de l'épaule en cas de destruction plus sérieuse de l'articulation; l'excision de la tête du radius et la synovectomie sub-totale dans certains cas d'arthrite du coude pour permettre d'éviter ou de remettre à plus tard l'arthroplastie, qui peut être exécutée par deux méthodes (a) semblable à l'excision classique de l'articulation ou (b) la réformation de l'extrémité inférieure de l'humérus et de l'extrémité supérieure du cubitus, recouvrant ces surfaces avec de l'aponévrose. Dans le rhumatisme articulaire la première de ces méthodes est la meilleure. L'excision de l'extrémité inférieure du cubitus avec fusion radio-carpe dans la position permettant la meilleure fonction possible est préconisée pour combattre la déformité du poignet et rendre la pronation et la supination. Les articulations des doigts et des orteils peuvent être corrigées par la résection des extrémités des os et la capsulectomie.

Pour l'extrémité inférieure le meilleur traitement de la maladie bilatérale de la hanche est l'arthroplastie avec un moule de vitallium, qui peut être exécutée par quatre méthodes: 1° l'arthroplastie de routine, 2° l'opération de Whitman modifiée, 3° l'opération de Colonna modifiée, 4° l'arthroplastie de la diaphyse supérieure ou arthroplastie intertrochanterique. Pour ces opérations l'essentiel est de connaître la technique, d'employer des gouges et des alésoirs spéciaux et de pratiquer des soins postopératoires minutieux.

Dans les kyphoses dorsales l'ostéotomie spinale lombaire corrige très bien la déformité, mais l'opération demande une exécution soignée et habile.

Les remarques de l'auteur sont basées sur l'expérience obtenue pendant son travail avec le Dr. Smith-Petersen au Massachusetts General Hospital, Boston, U.S.A.

КОНСПЕКТ.—Боль, искривления и немощность, которые являются следствием ревматического артрита и анкилозного спондилита, должны быть лечимы одновременно терапевтом, специалистом по физической медицине, ортопедическим хирургом и в некоторых случаях также и специалистом по глубоким Рентгеновским лучам.

Принцип полного отдыха для облегчения боли должен быть соединен с методами предназначенными для сохранения и восстановления функции.

Множественные суставные искривления в таких случаях вызывают необходимость длительного курса реконструкционного и функционального лечения, для которого необходимо полное содействие со стороны больного для интенсивного послеоперационного курса телесных упражнений.

Для верхней конечности предложены следующие операции: полное удаление акромиального выступа вместе с *bursa subacromialis* для дозволения свободного движения между центральным сухожилием дельтоида и сухожилистой лопаточной плеча, или же артродезис плеча в случаях серьезного повреждения сустава. В некоторых случаях артрита локтевого сустава, полное удаление головки radius и субтотальная синовектомия могут сохранить функцию сустава и даже устранить или временно отсрочить необходимость артропластики. Последняя может быть произведена двумя способами: 1) на подобие вышеописанного удаления сустава, или же 2) путем переобразования нижнего конца плечевой кости и верхнего конца локтевой кости и обшивания этих поверхностей фасцией. Первый способ предпочтается в случаях ревматического артрита. Для предупреждения искривления кистевого сустава и для восстановления пронации и супинации, рекомендуется полное удаление нижнего конца локтевой кости вместе со слипшимся лучевой костью с кистью в наилучшем положении для функции. Пальцевые суставы на руках и ногах могут быть исправлены резекцией концов костей и капсулектомией.

В нижних конечностях двухстороннее вовлечение бедренного сустава лучше всего лечить артропластикой при помощи витальной формы,—операция, которая может быть произведена четырьмя способами: 1) путем обыкновенной артропластики; 2) путем видоизмененной операции Витмана; 3) путем видоизмененной операции Колонна; и 4) путем интертрокантерной артропластики. Эти операции требуют, во-первых, знания оперативной техники и, во-вторых, употребления специальных бедренных инструментов для выдалбливания и рассверливания, а также тщательного послеоперационного надзора.

Для дорсального кифоза спины, спинная остеотомия на уровне поясницы дает прекрасное исправление, но эта операция должна быть произведена осторожно и искусно.

Автор основывает свои заметки на опыте, приобретенном в Массачусетской клинике доктора Смит-Петерсон, в Бостоне, Соединенные Штаты.

EXTRACTO.—El dolor, las deformidades ó la imposibilidad física a consecuencia de artritis reumatoidea ó espondilitis anquilosante, deben ser tratados por un equipo compuesto de un internista, un experto en fisioterapia, un cirujano ortopedista y, en ciertos casos, por un radiólogo, todos trabajando simultaneamente.

El "reposo" como medida fundamental para aliviar el dolor, ha de combinarse con métodos destinados a conservar ó restaurar la función.

Cuando las múltiples deformidades articulares exigen un largo tratamiento reconstructivo ó funcional, el éxito está vinculado a la sincera colaboración del paciente durante el régimen de ejercicios postoperatorios.

Los procedimientos recomendados para el miembro superior, comprenden: resección del acromion y de la bolsa subacromial, para proporcionar amplia movilidad entre el tendón proximal del deltoides y el ligamento capsular del hombro; artrodesis del hombro cuando la destrucción articular es más severa; en ciertos casos de artritis de codo, la resección de la cabeza radial, con sinovectomía, puede preservar la función articular y evitar ó retrasar la necesidad de una artroplastia, la cual, si llega el caso, puede llevarse a cabo: (a) como en una resección articular corriente, ó (b) remoldeando el extremo inferior del húmero y el superior del cúbito y recubriendo las superficies con fascia. El primer método es el de elección en los casos de artritis reumatoidea. Para vencer las deformidades de la articulación de la muñeca y restaurar los movimientos de pronación y supinación, se recomienda la resección del extremo inferior del cúbito y soldadura radio-carpal en posición de óptima función. Las articulaciones de los dedos de las manos y de los pies, pueden ser corregidas por resección de los extremos óseos y capsulectomía.

La artroplastia con casquete de vitalium es el mejor tratamiento a emplear cuando la articulación de la cadera está afectada bilateralmente. Pueden seguirse cuatro técnicas: (1) Artroplastia corriente; (2) Procedimiento de Whitman modificado; (3) Operación de Colonna modificada ó (4) Artroplastia

intertrocantérea. Es esencial en éstas operaciones conocer bien la técnica, usar gubias de cadera y escarizadores especiales y prestar cuidadosa vigilancia postoperatoria.

Para cifosis de la espina dorsal, la osteotomía a nivel de las vértebras lumbares proporciona una corrección excelente, pero es una operación que exige ser ejecutada con gran cuidado y habilidad.

Las observaciones de los autores son fruto de la experiencia obtenida trabajando con el Dr. M. N. Smith-Petersen en el Massachusetts General Hospital, Boston, Estados Unidos.

In recent years the orthopædic surgeon has been taking a greater share in attempting to overcome the pain, deformities and disabilities resulting from rheumatoid arthritis and ankylosing spondylitis.

A high standard of team-work is essential throughout the course of treatment, the team being composed of physician, physical medicine expert, orthopædic surgeon, and, in certain cases, deep X-ray therapist.

The commonly accepted treatment has been the avoidance of operations during the acute stage of rheumatoid arthritis, and the principle of rest is still the basis of all so-called "conservative" treatment. The aim of all treatment must be to relieve pain, to arrest the disease process and to preserve or restore function, and though rest treatment may help in relieving pain and arresting local disease, it may be harmful as regards restoration of function, particularly if, by putting one joint at rest, there is interference of function in the other joints of the limb.

The preservation of joint function is also hindered by muscle and bone atrophy, loss of ligamentous elasticity, and muscle spasm, which may be accompanied by fasciitis and bursitis, the result of friction between bone and muscle. It is essential to eradicate these secondary changes as a preliminary to any joint reconstruction, which itself should be considered before there are advanced destructive changes and before the bone is so atrophied and the surrounding soft tissues so fibrous that attempted movement between new joint surfaces merely results in further distortion.

Whilst the patient is undergoing surgical treatment a careful balance must be drawn, therefore, between rest and active exercises, pain being controlled, if necessary, by medication.

In many rheumatoid cases there are multiple joint deformities necessitating a long programme of reconstructive or functional treatment, and therefore requiring patient and persistent co-operation in the post-operative regime. The patient may also have to undergo one or more revisions of these operations in order to obtain a satisfactory end-result.

Prior to carrying out major reconstructive operations, it is important to remove foci of infection, to overcome anæmia, if necessary by blood transfusion, and to combat the tendency to infection in the poorly nourished tissues by an umbrella of penicillin.

As adjuncts to the operations such surgical measures as traction, plaster casts, with or without wedging or turnbuckle devices, braces, Gatch beds or plaster beds, are extensively employed and are of proved value.

Joint aspiration for effusion is particularly indicated in cases with a "joint-cycle", for instance pain in the knee one day, gross effusion the next, tendency to subside on the third day, followed by a quiescent period of eight or ten days.

My own personal series of cases treated along these lines is small, but during 1946 while working at the Massachusetts General Hospital, Boston, I had ample opportunity of studying many cases on the arthritic service of Dr. Walter Bauer and on the orthopædic service of Dr. M. N. Smith-Petersen.

Temporo-mandibular arthroplasty, by resection of the condyles of the mandible, enables patients to eat and talk more easily and is a very effective procedure, but recession of the mandible is likely to occur, with aspiration of the tongue during sleep, and in one case—following the operation on the second side—a tracheotomy was required.

It is possible to obtain a two-inch separation of the jaws with maintenance of molar apposition. This operation may be an essential preliminary to further procedures which require intubation for anæsthesia.

(1) *Upper limb procedures*.—A painful *shoulder-joint*, with adduction and internal rotation deformity at the gleno-humeral joint, is commonly seen in rheumatoid arthritis, and the accompanying muscle spasm is associated with a subacromial bursitis, which in time limits scapular movement, so that both components of shoulder movement are restricted.

Excision of the acromion process.—Acromionectomy—or acromioplasty as it is termed—together with removal of the villous subacromial bursa, eliminates the source of pain as well as allowing free movement between the central tendon of the deltoid and the tendinous shoulder cuff. Relief of pain also helps to relieve muscle spasm so that both gleno-humeral and scapulo-thoracic components of shoulder-joint function are improved.

The acromion process is osteotomized at the posterior margin of the acromio-clavicular joint, which may be left intact, though regrowth of the process appears to be less likely if the line of separation is taken through the joint itself. In closing the wound it is important

to suture the central tendon of the deltoid to the periosteal attachment of the trapezius muscle.

Where there is a more severe destruction of the shoulder-joint and the scapular muscles are adequate, arthrodesis of the gleno-humeral joint in a position of slight forward flexion, slight external rotation and about fifty degrees abduction provides good function. Care must be taken that excessive abduction is avoided, so that the arm can be adducted completely to the side, with rotation of the scapula.

(2) In rheumatoid arthritis of the elbow-joint spasm of the biceps muscle is a pronounced feature together with pain and restriction of movement, particularly pronation and extension. Smith-Petersen has drawn attention to the fact that the radial head may be drawn upward to impinge upon the capitellum so as to produce a joint defect. Excision of the head of the radius overcomes such faulty joint mechanics, and also enables a subtotal synovectomy to be performed with the result that pain is relieved, there is considerable improvement in the range of pronation, and a lesser increase in the range of flexion and extension.

The earlier this operation is performed, the better the functional result, and the greater the likelihood of avoiding complete joint ankylosis necessitating the more complicated arthroplasty procedure.

Formal arthroplasty of the elbow-joint with excision of the lower end of the humerus and upper ends of the radius and ulna is indicated when there is gross joint destruction or complete ankylosis. In traumatic cases a somewhat flail joint is likely to result, but in rheumatoid arthritis, owing to the loss of elasticity and fibrous contracture of the periarticular structures, a greater degree of stability is attainable, and therefore a more powerful limb.

This arthroplasty can also be performed by reshaping the lower end of the humerus and coronoid fossa of the ulna, excising the radial head and synovial membrane. The newly-shaped bone surfaces may be covered with fascia obtained from the fascia lata of the thigh or the triceps expansion. This method appears to provide greater stability, though there may be greater difficulty in obtaining more than the mid-range of mobility.

(3) The characteristic wrist-joint deformity is that of ulnar deviation with loss of dorsiflexion and rotation, which may be even further limited if there is also elbow-joint involvement. A useful procedure for restoring function of the wrist and hand is to excise the lower end of the ulna, and arthrodesis the radiocarpal joint in the position of maximal function—about twenty degrees of dorsiflexion. The whole procedure can easily be performed through an ulnar approach and markedly benefits pronation and supination as well as eliminating pain. In some cases, when deformity is minimal, it may be justifiable to excise the distal end of the ulna alone, thus enabling movement to be restored and eliminating pain in the inferior radio-ulnar joint.

The following is a brief outline of some of my cases:

I.—A. M., male, aged 37.

Eighteen years—psoriasis on elbows and knees. Treated also for trachoma. Fifteen months—painful swollen wrist-joints treated by gold injections. Nine months—involvement of feet, ankles, knees and elbows.

Pre-operative conditions.—Both wrists: Complete ankylosis in excessive dorsiflexion; pronation and supination limited to a few degrees only. Marked finger deformity.

Shoulders: Abduction 50 degrees. Complete loss of external rotation. 15 degrees internal rotation.

Operations.—June 1947: Excision of lower end of ulna and arthrodesis of left wrist. Excision of right acromion process. Excision of lower end of ulna and arthrodesis of right wrist.

July 1947: Excision of left acromion process.

November 1947: Sound fusion of right wrist and almost complete fusion of the left radiocarpal joint. Pronation, supination and rotation: Left 90 degrees; Right 120 degrees.

Shoulder movements	Left	Right	Shoulder movements	Left	Right
Abduction	90 degrees	160 degrees	External rotation ..	45 degrees	45 degrees
Forward flexion ..	160 degrees	160 degrees	Internal rotation ..	90 degrees	90 degrees

Improved function with less pain in elbows and fingers.

II.—R. H., male, aged 42.

1936: Onset of rheumatoid arthritis; widespread involvement. Ulnar deviation and flexion deformity of fingers. Wrist-joints ankylosed in slight flexion and radial deviation. Elbow-joint ankylosed at 60 degrees flexion on left and 160 degrees on right. Shoulder-joints, abduction on right to 45 degrees and to 35 degrees on left. Knees and hips, small range of movement only.

1947: Excision of right acromion process and lower end of right ulna. Arthroplasty of left elbow-joint. Right wrist: Pronation 45 degrees; supination 5 degrees. Right shoulder: Abduction 65 degrees—able to feed himself and place right hand behind the head. Left elbow: Range of movement 165 degrees to 85 degrees but following an accidental blow diminished to 155 degrees to 140 degrees with recurrence of pain and swelling.

Rheumatoid arthritis frequently attacks the metacarpophalangeal and interphalangeal joints primarily, or these joints may be involved secondarily to wrist, elbow or shoulder. In the latter case functional treatment directed towards the principal joint concerned may alleviate finger disability, but as a rule the combination of muscle spasm and gravity tends to produce characteristic disabling deformity of ulnar deviation, flexion and subluxation, and a stage may be reached relatively early when function can only be restored by operative surgery. Arthroplasty, consisting of resection of the bone ends and capsulectomy is useful for the metacarpophalangeal joints of thumb and fingers. Smith-Petersen has devised vitallium cups or moulds for these joints along the same lines as the hip mould, and has used them in a few cases, and some surgeons use fascia lata as an interposition substance; but whatever technique is employed it is essential to ensure correct post-operative rehabilitation and co-operation in the exercise regime on the part of the patient. As an alternative to arthroplasty, the metacarpophalangeal joint of the thumb may be arthrodeseis in a position of abduction and opposition. This procedure replaces a painful unsound ankylosis by a painless stable fusion against which the fingers can work to produce an adequate grasp.

(4) In the *lower limbs* the hip- and knee-joints frequently demand surgical treatment for pain and deformity associated with a variable degree of ankylosis, but measures to improve function are only indicated if the patient is willing to co-operate in a prolonged post-operative exercise regime. This is essential to restore muscle power and ligamentous elasticity, in addition to the contours of new joint surfaces, according to the principle of Wolff's Law, structure being adapted to function. Where the patient's morale is low and the muscles are markedly wasted and fibrotic, and particularly if there is unilateral involvement, stabilizing procedures such as arthrodesis may be indicated to relieve pain and enable weight-bearing in a sound mechanical manner. Unfortunately, in too many cases, the problem of bilateral painful stiff hips and/or knees has to be faced, and in these cases a strong plea is made for reconstructive operation before fibrosis of muscles and ligaments, and atrophy of bones, or joint degeneration have progressed too far. Even then, it is advisable to warn the patient that one operation may be insufficient to obtain the desired end-result, and that one or more revisions of the operation may be required to increase range of movement and enable the muscles to redevelop.

Smith-Petersen stresses this point forcibly with particular reference to vitallium mould arthroplasty of the hip-joint, and in a series of 25 cases reviewed personally, revision of the operation was required in 9 cases for loss of movement due either to bone proliferation, fibrous or bony ankylosis or faulty relationship of the mould, and 4 additional cases were revised for post-operative sepsis.

At revision, particularly if this is performed several years after the original arthroplasty, the effects of even limited function in the reformation of the joint are striking. The femoral head and the floor of the acetabulum are lined by smooth glistening cartilage, covered by thin synovial membrane, and the bone itself is sound and hard, in complete contrast to the soft, even putty-like bone, which is so frequently found at the first operation in these rheumatoid hip-joints. The vitallium mould retains its smooth gleaming surfaces throughout, being quite inert, and allowing the natural process of repair and reconversion to proceed unhindered in the hæmatoma around the femoral head and acetabulum, both of which have been re-fashioned at the level of raw bleeding bone.

Arthroplasty of the hip using fascia lata as an interposition substance was rarely very successful in rheumatoid arthritis, but the Smith-Petersen method with a vitallium mould, and the formation of a large deep acetabulum congruous with the femoral head, is of definite value.

In 1939 Dr. M. N. Smith-Petersen announced his technique of performing arthroplasty of the hip, his aim being to "create all the elements that make up a joint—joint surfaces, surface covering, and joint capsule". The inert mould enables organization of the surrounding blood-clot to form a joint capsule after congruous joint surfaces have been fashioned. Prior to vitallium in 1938, glass, viscaloid, pyrex, and bakelite had been used, experimental work extending as far back as 1923, and it was shown both by joint exploration and histological examination that the newly-formed joint surfaces consisted of fibro-cartilage, with areas resembling hyaline cartilage, covered by a true synovial membrane, which lined the new fibrous tissue capsule, and contained synovial fluid. Originally a two-stage procedure was the intention, but the inertness of vitallium has made the second stage of mould removal unnecessary, the mould becoming a "permanent insurmountable barrier to recurring ankylosis" (Smith-Petersen).

This clearly is an important advancement on such materials as Beer's membrane or pig's bladder, and fascia lata, with which there was a high incidence of recurring ankylosis, as well as further absorption of the femoral head and neck. Any hip-joint reconstruction must aim at producing a joint which is painless, stable, and capable of bearing weight. This form of

arthroplasty aims also at the restoration of a satisfactory range of movement, and thereby good function with return of muscle power.

The response to the procedure is in proportion to the degree of muscle wasting and other joint involvement, but even in the most severe bedridden cases it is usually possible to obtain enough hip-joint movement to allow of the sitting position and tripod locomotion with crutches. In addition the diminution of pain and muscle spasm, even though there may be contracture of the soft tissues, is of very real value to these patients.

In a few patients the increased use of the hip-joints results in knee-joint pain and effusion. This is temporary in nature and resolves with graduated exercises, as the circulation and muscle tone and power improve. Increased activity of the hip-joint following arthroplasty may also enable other joints to be spared the more severe effects of the disease process, owing to improved blood supply and muscle action.

In one case of rheumatoid arthritis involving the hip-joint a basal femoral neck fracture was sustained, and non-union resulted owing to the ankylosis of the femoral head in the acetabulum. Treatment by bone grafting of the fracture and performing mould arthroplasty resulted in union of the fracture and satisfactory hip-joint movement.

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2-3	..	47	2	1	—	1
3-4	..	62	5	5	—	—
4-5	..	43	2	1	—	1
Over 5	..	88	3	3	—	—

There are certain special technical points of importance in performing vitallium mould arthroplasty for rheumatoid arthritis of the hip-joint. It is advisable to make the new acetabulum larger and deeper, with a correspondingly large size of mould or cup which is freely movable in the new acetabulum and on the re-shaped femoral head. The greater part of the bone removal is from the acetabulum which is deepened to the inner pelvic cortex and made exactly congruous with the head by the use of special gouges and reamers devised by Smith-Petersen. The joint capsule and synovial membrane are excised completely, together with the rheumatoid pannus overlying the articular surfaces and margins of the femoral head and acetabulum, and any raw bone areas not covered by the vitallium mould are coagulated by diathermy in order to diminish the likelihood of new bone formation which would distort or re-ankylose the joint. Rheumatoid bone is soft and vascular so that blood loss may be severe during the gouging and reaming stage of the operation. This is counteracted by transfusion during the operation and as much as three pints may be necessary to maintain the hæmoglobin level. The atrophic nature of the bone and the desirability of obtaining a free range of movement may necessitate modification of the ordinary arthroplasty procedure. There are four types of reconstruction to consider:

(a) The routine arthroplasty in which the femoral head and the enlarged and deepened acetabulum are reshaped, made smooth and congruous, and a vitallium mould or cup is fitted in such a manner that movement is permitted both between the femoral head and the cup and between the cup and the acetabulum and yet a stable relationship is retained.

The complete excision of the joint capsule and synovial membrane, together with the rheumatoid pannus is also an important earlier step in the operation and may provide the explanation of the minimal pain suffered by these cases in both the early and later post-operative periods.

III.—A. C., male, aged 32.

1940: Onset of ankylosing spondylitis—pain and stiffness in spine. Plaster jacket and infra-red treatment.

1946: Progressive stiffness of both hips and pain. Deep X-ray therapy—no relief. Bilateral 30 degrees flexion deformity of both hips.

1947: May: Vitallium-mould arthroplasty of left hip. June: Vitallium-mould arthroplasty of right hip. December:

Hip-joint Movements	Right	Left	
Permanent flexion ..	20 degrees	10 degrees	Free from pain.
Flexion	45 degrees	50 degrees	Walking well with crutches—to transfer to walking sticks. Climbs stairs. Puts on own shoes and socks.
Abduction	20 degrees	20 degrees	
Adduction	10 degrees	10 degrees	He has a degree of dorsal kyphosis which at some future date may require treatment by spinal osteotomy.
Internal rotation ..	5 degrees	5 degrees	
External rotation ..	5 degrees	5 degrees	

IV.—S. R., male, aged 26.

1944: Treatment for "fibrositis" of back.

1944: Diagnosed as ankylosing spondylitis—no response to vaccine therapy.

1946: Complete ankylosis of dorsal and lumbar spine, and both hip-joints: knees partially involved. Doing clerical work in erect position.

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Hip-joint Movements	Right	Left
Flexion	50 degrees	50 degrees
Abduction	10 degrees	10 degrees
Adduction	10 degrees	10 degrees
Arc of rotation (about neutral) ..	10 degrees	10 degrees

(b) *The modified Whitman* type of operation is indicated if the femoral head has undergone atrophy or the bone is so soft that in the course of reshaping it by gouging and more particularly by reaming, bone is lost to such an extent that the femoral neck is too short. The greater trochanter and its attached muscles are transposed down the femoral shaft either as a primary or secondary operation, thereby lengthening the neck over the proximal end of which the mould is applied.

(c) *The modified Colonna* operation has to be carried out if there has been a more severe degree of absorption or loss of the femoral head and neck. The muscles are detached from the greater trochanter which itself is gouged and reamed in conformity with the acetabulum and a suitable mould is fitted. Frequently it is essential to deepen the acetabulum by a vertical osteotomy of the roof margin in order to obtain a greater degree of stability between the mould over the greater trochanter and the acetabulum. The outer margin of the osteotomy is elevated laterally and the gap filled with iliac bone chips. This is a very effective method of obtaining a further half or three-quarters of an inch depth in the acetabular roof.

(d) Finally, if the greater trochanter is unsuitable for reshaping, the arthroplasty can be made at the level of the lesser trochanter—the proximal shaft or intertrochanteric arthroplasty. The reshaping is carried out as previously and if possible some degree of varus is obtained to encourage stability in the acetabulum, which itself can be deepened by the vertical osteotomy method.

These latter operations result in a loss of leg length, but this is of little significance in bilateral cases, and they do tend to produce more unstable joints than the simple arthroplasty procedure, but in cases of rheumatoid arthritis and ankylosing spondylitis owing to fibrosis in the periarticular structures and muscle spasm, the wider bone resection may be of definite value in preventing re-ankylosis, though this must be considered in conjunction with the likelihood of placing the various muscle groups at a mechanical disadvantage.

This latter type of reconstruction is somewhat similar to the Girdlestone and Stamm operations, though they are pseudarthroses and are more likely to remain unstable, in addition to requiring temporary or even permanent use of a walking caliper.

V.—W. S., male, aged 26.

Ten years' history of ankylosing spondylitis with complete fusion of both knees, hips, lumbar, dorsal, and cervical spine and restriction of shoulder movements.

October 1946: Excision of left femoral head and neck.

March 1947: Modified Colonna vitallium mould arthroplasty (right).

November 1947:

Hip-joint Movements	Right	Left
Flexion	35 degrees	45 degrees
Abduction	20 degrees	30 degrees
Adduction	10 degrees	15 degrees
Rotation	few degrees	20 mainly external

The left hip is still somewhat unstable and the limb is considerably shorter than the right.

arthroplasty aims also at the restoration of a satisfactory range of movement, and thereby good function with return of muscle power.

The response to the procedure is in proportion to the degree of muscle wasting and other joint involvement, but even in the most severe bedridden cases it is usually possible to obtain enough hip-joint movement to allow of the sitting position and tripod locomotion with crutches. In addition the diminution of pain and muscle spasm, even though there may be contracture of the soft tissues, is of very real value to these patients.

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Adduction	10 degrees	15 degrees
Rotation	few degrees	20 mainly external

The left hip is still somewhat unstable and the limb is considerably shorter than the right.

arthroplasty aims also at the restoration of a satisfactory range of movement, and thereby good function with return of muscle power.

The response to the procedure is in proportion to the degree of muscle wasting and other joint involvement, but even in the most severe bedridden cases it is usually possible to obtain enough hip-joint movement to allow of the sitting position and tripod locomotion with crutches. In addition the diminution of pain and muscle spasm, even though there may be contracture of the soft tissues, is of very real value to these patients.

In a few patients the increased use of the hip-joints results in knee-joint pain and effusion. This is temporary in nature and resolves with graduated exercises, as the circulation and muscle tone and power improve. Increased activity of the hip-joint following arthroplasty may also enable other joints to be spared the more severe effects of the disease process, owing to improved blood supply and muscle action.

In one case of rheumatoid arthritis involving the hip-joint a basal femoral neck fracture was sustained, and non-union resulted owing to the ankylosis of the femoral head in the acetabulum. Treatment by bone grafting of the fracture and performing mould arthroplasty resulted in union of the fracture and satisfactory hip-joint movement.

The accompanying table shows the range of movement attained in the series of reviewed cases and the value of the operation both to the patient and to the surgeon.

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Years after operation		Average flexion range (degrees)	Satisfactory (No. of cases)		Unsatisfactory (No. of cases)	
			To patient	To surgeon	To patient	To surgeon
0-2	..	44	20	17	3	6
2-3	..	47	2	1	—	1
3-4	..	62	5	5	—	—
4-5	..	43	2	1	—	1
Over 5	..	88	3	3	—	—

There are certain special technical points of importance in performing vitallium mould arthroplasty for rheumatoid arthritis of the hip-joint. It is advisable to make the new acetabulum larger and deeper, with a correspondingly large size of mould or cup which is freely movable in the new acetabulum and on the re-shaped femoral head. The greater part of the bone removal is from the acetabulum which is deepened to the inner pelvic cortex and made exactly congruous with the head by the use of special gouges and reamers devised by Smith-Petersen. The joint capsule and synovial membrane are excised completely, together with the rheumatoid pannus overlying the articular surfaces and margins of the femoral head and acetabulum, and any raw bone areas not covered by the vitallium mould are coagulated by diathermy in order to diminish the likelihood of new bone formation which would distort or re-ankylose the joint. Rheumatoid bone is soft and vascular so that blood loss may be severe during the gouging and reaming stage of the operation. This is counteracted by transfusion during the operation and as much as three pints may be necessary to maintain the hæmoglobin level. The atrophic nature of the bone and the desirability of obtaining a free range of movement may necessitate modification of the ordinary arthroplasty procedure. There are four types of reconstruction to consider:

(a) The routine arthroplasty in which the femoral head and the enlarged and deepened acetabulum are reshaped, made smooth and congruous, and a vitallium mould or cup is fitted in such a manner that movement is permitted both between the femoral head and the cup and between the cup and the acetabulum and yet a stable relationship is retained.

The complete excision of the joint capsule and synovial membrane, together with the rheumatoid pannus is also an important earlier step in the operation and may provide the explanation of the minimal pain suffered by these cases in both the early and later post-operative periods.

III.—A. C., male, aged 32.

1940: Onset of ankylosing spondylitis—pain and stiffness in spine. Plaster jacket and infra-red treatment.

1946: Progressive stiffness of both hips and pain. Deep X-ray therapy—no relief. Bilateral 30 degrees flexion deformity of both hips.

1947: May: Vitallium-mould arthroplasty of left hip. June: Vitallium-mould arthroplasty of right hip. December:

Hip-joint Movements	Right	Left
Permanent flexion ..	20 degrees	10 degrees
Flexion	45 degrees	50 degrees
Abduction	20 degrees	20 degrees
Adduction	10 degrees	10 degrees
Internal rotation ..	5 degrees	5 degrees
External rotation ..	5 degrees	5 degrees

Free from pain.
Walking well with crutches—to transfer to walking sticks. Climbs stairs.
Puts on own shoes and socks.

He has a degree of dorsal kyphosis which at some future date may require treatment by spinal osteotomy.

IV.—S. R., male, aged 26.

1944: Treatment for "fibrositis" of back.

1944: Diagnosed as ankylosing spondylitis—no response to vaccine therapy.

1946: Complete ankylosis of dorsal and lumbar spine, and both hip-joints: knees partially involved. Doing clerical work in erect position.

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Hip-joint Movements	Right	Left
Flexion	50 degrees	50 degrees
Abduction	10 degrees	10 degrees
Adduction	10 degrees	10 degrees
Arc of rotation (about neutral) ..	10 degrees	10 degrees

(b) *The modified Whitman* type of operation is indicated if the femoral head has undergone atrophy or the bone is so soft that in the course of reshaping it by gouging and more particularly by reaming, bone is lost to such an extent that the femoral neck is too short. The greater trochanter and its attached muscles are transposed down the femoral shaft either as a primary or secondary operation, thereby lengthening the neck over the proximal end of which the mould is applied.

(c) *The modified Colonna* operation has to be carried out if there has been a more severe degree of absorption or loss of the femoral head and neck. The muscles are detached from the greater trochanter which itself is gouged and reamed in conformity with the acetabulum and a suitable mould is fitted. Frequently it is essential to deepen the acetabulum by a vertical osteotomy of the roof margin in order to obtain a greater degree of stability between the mould over the greater trochanter and the acetabulum. The outer margin of the osteotomy is elevated laterally and the gap filled with iliac bone chips. This is a very effective method of obtaining a further half or three-quarters of an inch depth in the acetabular roof.

(d) Finally, if the greater trochanter is unsuitable for reshaping, the arthroplasty can be made at the level of the lesser trochanter—the *proximal shaft or intertrochanteric arthroplasty*. The reshaping is carried out as previously and if possible some degree of varus is obtained to encourage stability in the acetabulum, which itself can be deepened by the vertical osteotomy method.

These latter operations result in a loss of leg length, but this is of little significance in bilateral cases, and they do tend to produce more unstable joints than the simple arthroplasty procedure, but in cases of rheumatoid arthritis and ankylosing spondylitis owing to fibrosis in the periarticular structures and muscle spasm, the wider bone resection may be of definite value in preventing re-ankylosis, though this must be considered in conjunction with the likelihood of placing the various muscle groups at a mechanical disadvantage.

This latter type of reconstruction is somewhat similar to the Girdlestone and Stamm operations, though they are pseudarthroses and are more likely to remain unstable, in addition to requiring temporary or even permanent use of a walking caliper.

V.—W. S., male, aged 26.

Ten years' history of ankylosing spondylitis with complete fusion of both knees, hips, lumbar, dorsal, and cervical spine and restriction of shoulder movements.

October 1946: Excision of left femoral head and neck.

March 1947: Modified Colonna vitallium mould arthroplasty (right).

November 1947:

Hip-joint Movements	Right	Left
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Abduction	20 degrees	30 degrees
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The left hip is still somewhat unstable and the limb is considerably shorter than the right.

The post-operative regime for the four types of operation outlined is identical and is as follows:

The limb is suspended in a Hodgen splint and Pearson knee attachment with 5 lb. skin traction for four weeks. During this time attention is paid to rehabilitation of the musculature, and hip movement is also encouraged by the patient sitting up and lying down flat in alternate periods, for flexion and extension, together with knee flexion exercises. At the end of the fourth week, the traction is removed and roller-skate exercises are commenced for the abductor and adductor musculature. The skates are strapped on to the posterior aspect of the patient's ankles, and movement is carried out over a hinged platform, which can be inclined to increase resistance as the exercises progress. At the sixth week the patient is allowed up in a chair and progresses to exercise on a stationary bicycle, adjusting the seat for movement in flexion and extension. Walking is re-established best by using a walking machine prior to crutches and encouraging a goose-step type of gait initially. Crutches are maintained for three to six months, and during this time exercises are continued on a bicycle, by climbing stairs and by sideways and forwards jumping. Gait is improved and loss of Trendelenburg is achieved by paying considerable attention to the abductor muscles, and a walking-stick replaces the crutches as the patient's muscle power and stability improve.

Keeping a correct heel and toe movement with the hip pushed inwards towards the centre of gravity must be impressed upon the patient. Regular supervision is maintained for a period of at least two years, and the active co-operation of the patient in the regime is an important factor in obtaining a good functional result.

In cases where bilateral hip-joint reconstruction is indicated the ideal time to perform the second arthroplasty is two to three weeks after the first, thus quickly enabling both hip-joints to attain the same stage in the post-operative exercise regime, the rehabilitation programme being timed from the second arthroplasty. It is obvious that with two major operations following one another at such a short interval, great care must be taken in maintaining the patient's general condition, and in particular the blood picture. Prior to the second operation it is essential that the hæmoglobin level should be raised to as near 100% as possible.

Painful swollen *knee-joints* can always be rendered painless and stable by arthrodesis, but the retention of mobility is all the more desirable when adjacent hip- and ankle-joints are also involved in the disease. Formal arthroplasty of the knee, owing to the complex mechanics of the joint, has not yet reached as satisfactory a stage as in the hip, but in cases where the joint is grossly distended by synovial effusion, or the synovial membrane is thickened and villous, much can be achieved by excising the synovial membrane as completely as possible together with the semilunar cartilages. This procedure is particularly indicated in a joint undergoing periodic episodic derangement, with incomplete resolution between the attacks and consequent loss of extension. Meniscectomy (medial and lateral) allows increase in the joint space, the more so if hypertrophied fatty and synovial fringes are removed at the same time, and the partial synovectomy and posterior capsulotomy also aid in regaining extension. Internal derangement of the knee-joint, due to a meniscus lesion in a joint involved by rheumatoid arthritis, should certainly be treated by excision of the meniscus. When there is a severe and persistent flexion deformity with joint subluxation, posterior capsulotomy is only effective if combined with division of the posterior cruciate ligament, and even the lateral ligaments. Total synovectomy in these cases usually results in fusion of the knee-joint with loss of pain at the expense of movement.

In performing posterior capsulotomy difficulty may be experienced owing to dense adhesions and the proximity of the popliteal vessels. Subperiosteal stripping of the capsule off the posterior aspect of the femur may prove an easier and safer method, lengthening the hamstring tendons, if necessary, and draining for twenty-four hours owing to hæmatoma formation. Only gradual extension of the knee-joint should be done, in order to avoid over-stretching the tibial and peroneal nerves, which are kept under observation throughout.

Arthroplasty with removal and re-shaping of adjacent bone surfaces, which have been destroyed by the rheumatoid pannus, and the interposition of fascia lata or vitallium plates or moulds between the new bone ends, is only of value if the patient's morale and muscular system allow of intensive physical therapy in the post-operative period, as the stability, as well as the mobility, of the new joint is directly proportional to the muscle power of the quadriceps group in particular.

VI.—B. L., single girl aged 28. (Case of Dr. Smith-Petersen.)

At age of 9 years—involvement of hips, knees, shoulders and fingers.

Four distinct exacerbations with periods of relative quiescence only.

1941: November: Arthroplasty of left hip—vitallium mould. December: Arthroplasty of right hip—vitallium mould.

1942: October: Arthroplasty of left knee—vitallium mould. December: Arthroplasty of right knee—vitallium mould.

1944: Removal of mould from left knee.

1946: Removal of mould from right knee—all elements of a joint were present. November: 40 degrees flexion range in each hip. 20 degrees flexion range in left knee. 10 degrees flexion range in right knee.

Where pain and crepitus are prevalent in the femoro-patellar compartment of the knee in addition to X-ray evidence of destruction of the articular surfaces, excision of the patella together with any excessive villous synovial membrane is effective in reducing pain and maintaining function. It is important to make certain that the quadriceps apparatus is fully repaired, otherwise extensor lag and instability will interfere with knee-joint function. As a less radical alternative to complete excision of the patella, plastic operation on this bone, excising irregular or hypertrophic outgrowths and rendering it more congruous to the corresponding surface of the femur are of value, and it is possible that retention of a portion of the patella aids in repair and strengthening of the medial and lateral quadriceps expansions and consequently improves the quadriceps mechanism.

Pain, restriction in the range of movement and deformity of the *ankle-joint* are best treated by arthrodesis, fusion being obtained in about 10 degrees of equinus to allow for the heel on the footwear.

For pain and *fixed claw-toe* deformity of the *metatarsophalangeal joints*, excision of the metatarsal heads or bases of the proximal phalanges enables both the toes and metatarsus to be re-aligned and the metatarsal arch to be restored.

The operation is followed by a short period of immobilization in moulded plasters (two to three weeks), or toe correction may be maintained by intramedullary wires, and proceeds to a full active exercise regime. This is a useful method of treatment, but should be instituted before deformity is extreme and associated with secondary bursitis and fasciitis.

Adventitious bursæ should be excised together with abnormal bony excrescences, and neurectomy of the digital nerves should be performed if they have undergone neuritic changes or neuroma formation, thereby producing severe pain.

Spinal osteotomy is an operation devised by Smith-Petersen to enable the establishment of compensatory lumbar lordosis for severe kyphotic deformity of the dorsal spine. In one case both lumbar and dorsal osteotomies were performed, but Smith-Petersen is of the opinion that nothing was gained by the dorsal osteotomy. The patient believes to the contrary. This operation is performed in the lumbar region at levels showing a minimum of bony wedging, the excess bone formed in the interlaminar ligaments being excised together with wedges from the intra-articular facets in one or two stages at two or more levels. After detaching the ligamenta flava and passing a periosteal elevator anterior to the lamina and articular process, into the lateral intervertebral notch, the osteotomy is performed through the superior articular process of the vertebra above, in an oblique plane of 45 degrees with the frontal plane. The number of levels is determined by the extent of new bone formation in relation to the facets and intervertebral discs. Correction is then obtained by hyper-extending the spine so that the edge of the lamina above slides on a shelf of the lamina below, without compressing the cord or overstretching the soft tissues, particularly the femoral nerves and vessels. After satisfactory correction, spinal fusion is carried out by raising bone flaps from the laminae and using lamellæ from the spinous processes which were removed initially. The results of this operation are dramatic—one patient stating that he could see ahead for the first time in eighteen years—but it is a difficult operation, the spinal extension having to be carefully controlled. Post-operative distension and retention have to be anticipated being due possibly to stretching of the autonomic nerves. Later follow-up shows that these patients retain their improved position and are even able to discard their spinal support.

VII.—G. T., male, aged 37.

Twelve years—progressive pain and stiffness of spine with increasing flexion deformity. Recently pain in right hip, with flexion contracture. Severe dorsal kyphosis—when standing with knees straight the face is directed to the ground.

Blood sedimentation rate—39 mm. in one hour.

1947: July: Osteotomy of spine at lumbar 3 and 4 level. November: Spine soundly fused with compensatory lumbar lordosis. Now able to see 100 yards ahead. December: Able to see 20 yards ahead. Tendency to slump. For further correction, by spinal osteotomy at lumbar 2 and 3 level.

VIII.—G. M., female, aged 29.

Four years' history—ankylosing spondylitis treated by vaccine and deep X-ray therapy.

1947: July: Spinal osteotomy—excellent correction. August, September: Arthroplasty of left and right hips.

1948: January: Back soundly fused: wearing spinal support.

Hip movements:

Right hip: Flexion 50 degrees

Both hips: Abduction 15 degrees; Adduction

Left hip: Flexion 45 degrees

20 degrees; Arc of rotation 10 degrees.

No pain—walking erect with a good stride. Lumbar lordosis fully compensates dorsal kyphosis.

In conclusion I must stress that I have only summarized the place of reconstructive surgery in the treatment of the rheumatoid diseases, and have scarcely alluded to the various surgical measures employed for protective splintage, correction of deformity and arrest of the local arthritic process. In all phases of surgical treatment, however, it is essential to maintain a careful physiotherapeutic regime, with the emphasis on active exercise and muscle re-education, together with early movement of the newly reconstructed joint.

These major joint reconstructions are formidable operations, requiring courage and vision on the part of both patient and surgeon, but in many cases the benefit obtained is not only seen in the relief of pain, prevention of deformity and partial restoration of function, but in the marked improvement in the patient's morale and mental outlook, which is also an important factor in the treatment of rheumatoid diseases.

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The President (Dr. Tegner) expressed his interest in the patient described by Mr. Law who injured an elbow-joint on which an arthroplasty had been performed and who developed a flare-up of the rheumatoid condition in this joint. Could joints on which arthroplasties had been performed undergo recrudescences of rheumatoid arthritis as bad as or worse than joints which had not been subjected to operation?

Mr. Law had spoken of ankylosing spondylitis as though it were the same disease as rheumatoid arthritis. This was the common opinion in America but in this country it was more generally believed that they were different diseases. Could Mr. Law throw any light on this in view of the fact that he had described rheumatoid bone as being soft and vascular? Was spondylitic bone of the same texture?

Dr. Guy Beauchamp asked for details of technique in the transposition of the greater trochanter in the reconstruction of the femoral head.

Mr. Law, in reply to Dr. Tegner, said that recrudescences could occur in joints which had undergone arthroplasty, and must be treated according to first principles. He was in agreement with the British view that rheumatoid arthritis and ankylosing spondylitis are separate diseases. In the latter there is a complete bony ankylosis, the bone being vascular and well formed, and not so soft or easily cut as in rheumatoid arthritis.

In reply to Dr. Beauchamp, Mr. Law stated that the trochanter with the attached muscles is detached by an osteotome, transposed downwards and fixed to the femoral shaft on its outer aspect by means of a vitallium screw or wire sutures. If the trochanter is used for articulating with the acetabulum it is re-shaped and made congruous with the acetabulum using the special gouges and reamers.

Section of Orthopædics

President—GEORGE PERKINS, M.C., F.R.C.S.

[November 4, 1947]

Death from Homologous Serum Jaundice following Nail-Arthrodesis of the Hip.
Specimen of Right Hip-Joint shown.—W. D. COLTART, F.R.C.S.

The Conservative Treatment of Lumbar Disc Lesions.—E. J. CRISP, M.B.

The majority of lumbar disc lesions, with or without sciatica, generally recover completely if treated by adequate conservative measures. Bed rest, by itself, is insufficient. In hospital, the bed-making routine subjects the patient to considerable movement, while if treated at home he gets up for toilet purposes.

The lumbar spasm which develops after a disc injury is protective, and holds the spine in the optimal position both for the patient's comfort and to allow healing to take place, and it is essential that movement at the site of the lesion should be minimal.

By the application of a plaster jacket the natural processes of repair may be not only assisted, but accelerated. The plaster is applied with the patient standing in the position of greatest comfort, and it is important that no attempt should be made to correct deformity. Anteriorly the plaster extends from the xiphisternum to the pubis, posteriorly from the inferior angles of the scapulæ to the tip of the coccyx. The plaster is accurately moulded to the pelvis and the lower ribs, and is cut away at the groins to allow the patient to sit down. The plaster is light, comfortable and allows him to remain ambulatory.

The patient rests in bed until the pain is relieved, usually a matter of a few days only, after which he is allowed to get up, and in due course to return to his usual occupation.

It is essential that the plaster, or replaster, should be worn for upwards of three months to ensure sound healing. The object of the treatment is not only to bring about repair of the injured disc, but also to produce a fibrous ankylosis of the affected segment, and thus prevent further trauma. Adaptive shortening of ligaments and muscles at the site of the lesion restricts movement to a minimum, especially forward flexion. After removal of the plaster hyperextension exercises are given, but lumbar flexion is left to return spontaneously. A lumbar brace is worn for a further three months as a safety measure, and to give the patient confidence.

Three cases of acute sciatica following rupture of an intervertebral disc were shown, wearing plaster jackets. All three patients, a blacksmith, a tailor's cutter and a clerk, derived such complete relief from this form of treatment that they were able to return to work within seven days of the application of the plaster.

Amputation of Toes.—J. S. BATCHELOR, F.R.C.S.

When first seen this patient was complaining of severe pain in the left foot, chiefly over toes and under metatarsal heads.

Examination showed that the second and fourth toes had previously been amputated. The remaining toes were stiff and clawed and there were tender callosities under all metatarsal heads. Amputation of the remaining toes has produced complete relief of symptoms; the patient has been able to resume his work as a farm labourer wearing an ordinary boot.

Acromioclavicular Dislocation.—J. S. BATCHELOR, F.R.C.S.

This patient sustained a dislocation of the right acromioclavicular joint when serving in the Army, and developed pain in the region of the joint particularly on abduction of the arm. Excision of the distal end of the clavicle relieved these symptoms but was followed by pain in the ulnar border of the forearm and hand, apparently

due to pressure of the lower trunks of the brachial plexus on the first rib, as a result of dropping of the shoulder girdle. These symptoms were completely relieved by use of a modified "Böhler's" clavicle splint which elevated the shoulder girdle.

Calvé's Disease of the Spine.—G. W. E. LITTLE, M.B. (by permission of ERIC LLOYD, F.R.C.S.).

A boy aged 4 years and 4 months who was brought to Out-patients' Department with the complaint that he was holding his head to one side and inclined to hunch his shoulders in a peculiar manner when looking upwards. This had been noticed for some few weeks, but had been getting worse.

Past history.—October 1945, pain in right hip. X-ray showed erosion right iliac bone (? tuberculosis), Plaster of Paris spica applied. March 1946, X-ray showed erosion left ilium similar to condition of opposite side, ? calcium deficiency. Given a course of calcium therapy. Shortly after this he developed a stiff neck. He had a heavy cold at the time with some pyrexia, but this cleared up while the stiffness of his neck continued. X-ray showed a defect of the fifth and sixth dorsal vertebræ. May 1946, admitted to hospital for treatment and was an in-patient for nearly a year.

Present state.—On examination, weight 35 lb., height 3 ft. A healthy-looking young boy. No abnormality was discovered beyond a mild degree of torticollis due to tightness of the right sternomastoid. His hip and spinal movements all appeared normal and he did not complain of any pain or tenderness.

X-ray showed an unusual deformity in the upper thoracic region and further pictures showed this to be probably due to Calvé's disease of the spine. There is marked collapse of the fifth dorsal vertebra associated with widening of the intervertebral disc space. There is no loss of intervertebral disc spaces. There is apparently expansion of the abnormal vertebral body laterally and tendency to such expansion with slight wedging of the sixth dorsal vertebra (figs. 1 and 2). X-ray of the skull, ilia and other long bones showed no abnormality.



FIG. 1.



FIG. 2.

Calvé's disease of the fifth thoracic vertebra.

His blood chemistry was normal: Serum calcium 10.9 mg. per 100 c.c. Alkaline plasma phosphatase 15.2 units. Inorganic blood phosphorus 3.8 mg. per 100 c.c. Mantoux 1/1000 negative on two occasions. E.S.R. 15 mm. in one hour.

REFERENCES

- CALVÉ, J. (1928) *The Robert Jones Birthday Volume*, London, 315.
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Instability of the Longitudinal Arch.—A. G. APLEY, F.R.C.S.

History.—The patient is a first child born after a normal labour. At birth his head was small and he had a cyst on his back in the upper dorsal region. When he was 4 months old this cyst was removed. It is said to have been a dermoid. After this operation his head grew somewhat rapidly until it became larger than the average for his age. He sat up at 14 months and talked at 2 years. At the age of 2½ he was seen at an orthopædic hospital where he was diagnosed as hydrocephalus and bilateral pes calcaneo-valgus; the left foot was manipulated and put into plaster for a few months. Otherwise he had no treatment. The abnormally rapid growth of his head did not continue; in fact his mother says that from about the age of 3 it has scarcely grown at all.

He was first seen at St. Thomas's Hospital in August 1947 when he was aged 5, having never, up to that time, been able to walk.

Clinical findings.—The child has a large head, its circumference being 22 in. His facies are "adenoidal" in type and he seems rather backward (a condition which even his mother admits). His eyesight and hearing are normal, as also are the upper limbs, except for a small birthmark on the right arm. There is a scar in the mid-line overlying the upper dorsal spine where the cyst was removed. X-ray shows a bony defect in this area, but none elsewhere in the spine.

The feet: When the boy attempts to stand, both feet immediately collapse into marked valgus (fig. 1). The muscles, however, are all present and work; but they are not as strong as they should be at his age. The Babinski response is very definitely extensor on the right and probably extensor on the left.

Comment.—It seems more than likely that there is an underlying neurological condition to account for the lack of proper control of the feet. The rapid growth of the head following removal of the tumour from the upper dorsal spine suggests that this tumour might have contained a prolongation from the meninges.

Whatever the underlying neurological condition, the chief orthopædic interest lies in the feet. Why is it that although the muscles are under his voluntary control he is unable to stand normally? The suggestion is that he has never learnt how to stand; in other words he



FIG 1.

has failed to acquire a normal postural reflex so that, his muscles being unable to balance his body on his feet, his longitudinal arch collapses.

There is known to be some association between myelinization of the pyramidal tract and the acquisition of a flexor Babinski response. It is conceivable that such myelinization may, when it occurs, promote the development of the postural reflex.

Rotatory Frame for Plaster Beds.—E. T. BAILEY, F.R.C.S.

The frame consists of a wooden base of standard type with three cross bearers, which, instead of supporting the plaster shell direct, are grooved to take three circular discs. Each of these discs is divided into two halves, which are shaped to the respective anterior and posterior shells on their central aspect, leaving a complete circular periphery to rotate on the grooved frame. The nursing procedure to turn a patient consists of applying the anterior shell, followed by the three anterior halves of the

due to pressure of the lower trunks of the brachial plexus on the first rib, as a result of dropping of the shoulder girdle. These symptoms were completely relieved by use of a modified "Böhler's" clavicle splint which elevated the shoulder girdle.

Calvé's Disease of the Spine.—G. W. E. LITTLE, M.B. (by permission of ERIC LLOYD, F.R.C.S.).

A boy aged 4 years and 4 months who was brought to Out-patients' Department with the complaint that he was holding his head to one side and inclined to hunch his shoulders in a peculiar manner when looking upwards. This had been noticed for some few weeks, but had been getting worse.

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Section of Ophthalmology

President—HAROLD LEVY, F.R.C.S.

[November 13, 1947]

Two Cases of Iridocyclitis.—M. SARWAR, M.B.

I.—Mrs. A. has been attending the Oxford Eye Hospital since October 1946, complaining of eyes being sore off and on for two months and gradually getting blurred. She was diagnosed as chronic iridocyclitis.

On examination.—R.E.: Vision 3/60 not improved. Slight ciliary injection. Many mutton fat K.P. at the back of the cornea. Cells floating in the anterior chamber. Multiple posterior synechia and destruction of pupillary margin. Organized exudate on the anterior lens capsule. No nodules on the iris. Fundus not seen.

L.E.: Vision 6/18 not improved. Slight ciliary flush. Pigmented K.P. in the centre of the cornea. One posterior synechia. Pigment on lens capsule. No nodules on iris.

Neck: Swelling of thyroid. Thyroid gland is enlarged.

Hands: The finger joints of both hands are swollen.

Kahn and W.R. negative in blood tests.

X-ray of chest revealed enlargement of hilar glands and appearances of sarcoidosis. Bony changes in the hands compatible with sarcoidosis.

II.—Mr. E. First seen at the Oxford Eye Hospital in June 1942. Diagnosed as chronic iridocyclitis.

On examination.—R.E.: P.L. only. Eye white. Many mutton fat K.P. at the back of cornea. Anterior synechia. No cells in the anterior chamber. New vessels on the iris and remains of nodules. Pupillary margin bound down. Organized exudate on the anterior surface of the lens. Tension high. L.E.: No P.L. Clinical findings similar to right eye.

Abdomen: Liver enlarged two fingerbreadths. Spots on the abdomen similar to De Morgan's spots.

Kahn and W.R. negative in blood tests.

X-rays of chest show enlargement of hilar glands and appearances of sarcoidosis.

Mr. Sarwar said that he showed these cases because of the infrequency of the condition and because in this case there were hilar changes and other features compatible with sarcoidosis.

(1) A chronic form of iridocyclitis associated with arthritis, nodules on tendons, &c., and signs of sarcoidosis was first described by Jonathan Hutchinson in 1873.

(2) Iridocyclitis associated with sarcoidosis may be of three types: (a) the type usually described, i.e. with nodules on the iris; (b) with no nodules on the iris; and (c) an ordinary type of iritis which clears up without causing much damage to the eye.

(3) Large doses of cod-liver oil appear to be of benefit in such cases.

MAY—OPHTHAL. I

discs, locking these with a double-studded bolt and then, with the aid of, usually, one assistant, turning the patient gently, through 180 degrees when the bolts are undone and the posterior shell removed. (See Fig. 1.)

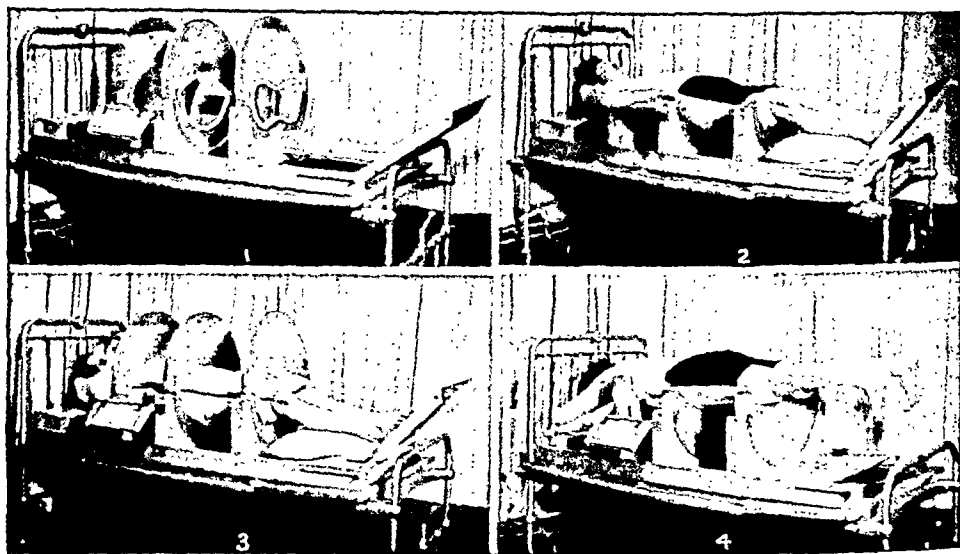


FIG. 1.

The frames can be used for successive patients by reshaping the discs to new plaster shells as required, leaving the main part of the frame and the circular periphery of the discs as a constant entity for all cases.

The frames, as originally designed at the Orthopædic Centre, Northern Hospital, Winchmore Hill, are now obtainable at the Carpentry Department, British Legion Industries (Preston Hall) Incorporated, Maidstone, Kent.

Talipes Calcaneo-varus with Extreme External Rotation of Tibiæ.—P. G. EPPS, F.R.C.S.

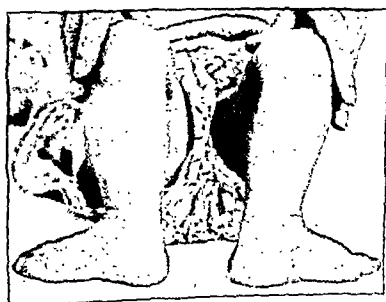


FIG. 1.

P. K., female, aged 2 years 3 months. The talipes was treated by manipulation and plaster followed by modified Denis Browne splints and good correction obtained. She has just started walking and stands with feet pointing almost directly laterally. There was delayed development of the patellæ, which do not show on X-ray, and are now only just palpable clinically. The hips are normal.

The photograph (fig. 1), taken at 1 year and 6 months, shows the deformity well. She has no other congenital defects. The deformity

will probably need to be corrected by rotation osteotomy of the tibiæ.

(The report of this meeting will be concluded in the next issue of the *Proceedings* of the Section of Orthopædics.)

III. Trachoma Chronicum Cicatricum.

Female, aged 60.

Both eyes: Trachoma chronicum cicatricum.

Right eye: Serpiginous ulcer nineteen years ago. Healed by graft from the mucosa of the lip (London Jewish Hospital).

Biopsy result: The specimen consists of connective tissue and its covering of stratified squamous epithelium. The epithelium, 8 or 9 cells thick, shows: (1) Basal cells, which are cubical or low columnar, and whose oval nuclei stain moderately with hæmatoxylin and contain a few deeply staining chromatin particles. (2) Intermediate polyhedral cells between which are cell bridges. (3) Surface cells which are flattened but not keratinized. (4) Adventitious cells—an occasional polymorphonuclear leucocyte.

The outline of the deep surface of the epithelium is somewhat undulating, presumably representing the succession of imperfectly formed papillæ and interpapillary downgrowths.

In addition there are seen in the sections two epithelial downgrowths, a small solid one extending horizontally just below the epithelium, whereas the other, which has a hollow cavity, extends vertically to the surface for a distance equal to three or four times the thickness of the usual epithelial layer.

The subepithelial tissue consists of loose connective tissue, appearing somewhat œdematous in places, and well supplied with blood and lymphatic capillaries. Just below the epithelium it is infiltrated with lymphocytes and plasma cells in considerable numbers, together with some endothelioid cells. Situated also in this tissue are a few tubulo-racemose glands, whose acini are lined by columnar cells with nuclei near the cell base, whilst an outer cell layer is formed of darker small cubical cells. These glands resemble buccal glands.

In the specimen, the structure of the original mucous membrane graft is maintained both in its epithelial and subepithelial parts.

[December 12, 1947]

CLINICAL MEETING HELD AT THE MOORFIELDS, CENTRAL AND WESTMINSTER OPHTHALMIC HOSPITAL, MOORFIELDS, LONDON

Eight cases by E. F. KING, F.R.C.S.

I. Intra-ocular Copper Wire Foreign Body in the Cornea and Chalcosis Bulbi.

J. M., aged 25.

This man first attended hospital 28.11.47 with a recent and trivial laceration of the right eyebrow. At the same time it was noticed that he had a hook-shaped piece of copper wire embedded in the right cornea, one end of which was projecting into the anterior chamber. He had no knowledge of injury to the eye.

There was well-marked chalcosis oculi, a "sunflower" cataract and metallic iridescent lustre of the anterior lens surface and Descemet's membrane. Vision of this eye was 6/5, and of the left 6/6.

On 3.12.47 the piece of copper wire was easily removed with the aid of forceps through a superficial corneal incision. There was no loss of aqueous and healing of the corneal wound was uneventful.

The interest in this case is the patient's total ignorance of the presence of the foreign body, and also the well-established chalcosis of the anterior segment with retention of normal vision.

Mr. J. H. Doggart said that this was certainly a beautiful case of a kind which one did not usually get a chance of observing, simply because the eye was usually more disorganized. Mr. King had spoken of the endothelium, but it was Descemet's membrane which had the bluish colour showing in this case the characteristic of being far more marked at the limbus and gradually fading towards the axial portion of the cornea. At one time in this case the polychromatic lustre was so marked that it was quite easy to appreciate it with a loupes, but it was now not nearly so brilliant, and he was not sure whether the "petals of the sunflower" were not a little stunted. His impression was that the superficial lens opacity was less marked than it had been before this operation.

Mr. J. D. M. Cardell referred to a case in which a piece of copper wire had entered the eye with some considerable force, penetrating the cornea and the anterior capsule, but remaining within the lens, within which its total length was accommodated. No change occurred in the eye for eighteen months. At the end of that time a cataract rapidly made its appearance, and, fortunately, the copper wire came away with the lens material when the lens was evacuated with a curette.

Mr. J. P. F. Lloyd said that he had observed one very striking point in one of these cases. The multiple peripheral anterior synechiae in this case were an appearance that he had not previously observed. The mechanism of production would seem to be that the sheer bulk of the lesions in the iris brought them far enough forward to cause them to adhere to the posterior surface of the cornea.

Mr. R. Affleck Greeves said he would like to ask two questions, the first as to whether or not the ocular disturbance could remain limited to one eye only, and the second whether the ultimate prognosis was uniformly bad. He remembered seeing a young man with severe iridocyclitis in one eye, whose lungs were pronounced to show the typical X-ray appearance of sarcoidosis, and in whom the other eye remained unaffected. After a prolonged period the iridocyclitis cleared up under local treatment.

Dr. Noah Pines wondered whether the possibility of a tuberculous origin had been eliminated.

Mr. D. V. Giri said that a man aged 42 occupying an important position in Eastbourne was sent to him in 1940 for a second opinion. He was a high myope. Mr. Giri himself gave him no treatment, but the case went under the care of one of his London colleagues and was diagnosed as sarcoidosis. Such treatment as he received—X-rays to the chest, short-wave diathermy and atropine to the eyes, &c.—made his general condition worse without improving the condition of the eyes. After the cessation of all treatment, in the course of a year or more, the eyes quietened down of their own accord and his general condition improved remarkably. The left cornea had turned opaque and the eye was practically blind, but the right eye improved sufficiently to enable him to fulfil his important duties and he was very active physically too. This case demonstrates that sarcoidosis has a tendency to spontaneous recovery both locally and generally over a period of years.

POSTSCRIPT (Dr. Sarwar) 26.4.48.—The nodules in sarcoid of iris really appear more solid, and as Mr. Lloyd says, are solid enough even to cause an irregularity at the limbus when they are at the periphery of the iris. So far as is known, sarcoidosis is a self-limiting and self-resolving disease, and it is quite possible to get one eye involved—the other eye escaping. I am grateful to Mr. Greeves for pointing this out.

Tuberculin tests have been found negative in this condition and were so in these two cases. There is no relative lymphocytosis in the blood, and no general reaction; these points fairly exclude ordinary tuberculosis. Whether sarcoidosis is due to attenuated tuberculosis or not is not definitely settled yet.

The main danger of sarcoidosis in the iris is the pathological changes which it leaves behind. The disease process is cured sooner or later, but sequela-like posterior and anterior synechiae and persistence of big thick K.P. which may not absorb result in the functional destruction of the eye usually to a greater rather than a lesser extent. Mr. Giri's case must be counted as one of the fortunate ones where less interference has resulted.

Three Cases by NOAH PINES, M.B.

I. Trachoma Chronicum Cicatricum.

Mr. A. S., aged 54.

Both eyes: Trachoma chronicum cicatricum.

Right eye: Denig's operation twelve years ago (1935) (London Jewish Hospital). The middle part of the graft did not take. The end of the graft (at 3 o'clock) was removed and sent for investigations.

My thanks are due to Mr. Eugene Wolff, F.R.C.S., and to Mr. W. H. Gordon, Assistant Pathologist, Royal Westminster Ophthalmic Hospital, who kindly examined the specimen and reported as follows:

The epithelium throughout the section is stratified squamous, without cornification. It is not of uniform thickness, being much thicker over one-half of the section; the thicker half shows slight oedema of the prickle-cell layers (acanthosis). The papillae are stunted for the most part, though in the area of thin epithelium there are one or two considerable downgrowths of epithelium, which, however, remain quite regular in arrangement. The immediately subepithelial connective tissue is fairly close-fibred and in only one place (in the thick epithelium area) is there slight round-celled infiltration. The deeper connective tissue is looser and vascular.

The characters of the whole graft therefore are those of mucous membrane, slightly modified by stunting of the papillae, and, in part, by acanthosis.

II. Pannus Crassus ? Trachoma.

Mrs. A., aged 60, presented herself at Moorfields Hospital on 3.12.45 with a papilloma of the left upper lid. Biopsy revealed a granuloma. It later changed to a rodent ulcer and repeated biopsy revealed chronic conjunctivitis. Treated with penicillin without success. Now the upper lid is swollen, the tarsal plate thickened, the conjunctiva bulbi, as well as of the lids, are grossly inflamed. My thanks are due to Miss Ida Mann for supplying the previous history.

siderosis of this eye and pupillary dilatation was evident. The *left eye* showed well-marked siderosis of both anterior and posterior segments. There was a small sub-conjunctival foreign body on the nasal side about 9 mm. posterior to the limbus. Pupillary dilatation was limited in this eye, and the vitreous was too cloudy for any fundus details to be noted. The lens of each eye was found to contain congenital, grey and brownish dot- and club-shaped opacities throughout the cortex, chiefly distributed equatorally. The siderosis of the left eye had not noticeably altered the colour of these opacities in this eye, compared with the other eye, although there was anterior subcapsular rust-coloured deposit.

X-ray showed no radiopaque foreign bodies in the right eye, but a well-defined radiopaque foreign body in the left eye situated in the oral region in the 7 to 8 o'clock meridian.

At operation 7.11.47 a magnetic intra-ocular foreign body was removed from the vitreous through a posterior radial incision into the pars plana in this meridian. The ferrous metallic fragment was considerably decomposed, and, following it from the vitreous came three pieces of whitish plaster or concrete, similar to the pieces on the right iris.

The removal of these four distinct fragments from the vitreous is excellent evidence of the value of posterior route removal, as it would not have been possible by the anterior route, and, at the same time, proves that the foreign bodies in both eyes were the result of the explosion in 1940. It was not proposed to touch the foreign bodies in the right eye.

Examination in February 1948 showed that the left eye was already much improved. The patient states that he can now read the paper with the left eye, and vision is 6/36. The vitreous is much clearer. The pupil has already regained its full dilatation, which exposes previously unseen peripheral siderotic subcapsular spots in the lens. There was no retinal detachment, and no intra-ocular ill-effects could be observed from the operation. It is expected that the condition of this eye will improve still further. The rusty colour of the iris is already fading and now more nearly resembles that of the right eye.

The President said that he was aware of a similar type of case in which a man got a certain amount of concrete mixture in his eye. The anterior chamber was full of concrete particles, but the eye did not get very much inflamed, it quietened down, and he kept a fair amount of vision.

VIII. Macular Changes in Both Eyes in a Child Aged 7 Years.

Mr. A. J. B. Goldsmith said that the case reminded him very much of the description of toxoplasmal chorio-retinitis given by Colonel Derrick Vail in a Paper read before the Section in 1943 (Vail, D., *Proc. R. Soc. Med.*, 36, 629) and he wondered if the possibility had been considered. This condition typically gave rise to a bilateral macular choroiditis; it was, however, rare, very few cases having been described on the Continent of Europe, and not very many in America. The choroiditis in these cases was due to infection by toxoplasma, a protozoal parasite; the infection was thought to be transplacental from a mother who might herself show no stigmata of infection except perhaps a positive serological reaction. In the infant it was usually fatal, but occasionally the infection died out leaving as permanent evidence various forms of eye defect and, usually, calcified foci in the choroid of the ventricular system of the brain. He thought it would be worth while doing an X-ray of the skull and perhaps, serological tests.

Two Cases by A. G. CROSS, F.R.C.S.

I. Bilateral Aniridia, Glaucoma and Lens Opacities in a Woman.

Mr. A. J. B. Goldsmith asked whether the genetics in this case had been considered. The patient had told him she had two daughters who showed the same condition, although apparently her own parents were normal.

Mr. Cardell suggested that benefit might be obtained by tattooing the cornea in successive quadrants. He had had a case or two which had benefited. The tattooing might be so regulated as to be of a dark brown colour.

II. Band-keratitis in Man Aged 45.

Mr. J. Minton said that this might eventually become a compensation case. It would be very difficult for the ophthalmologist to decide whether it was an occupational disease or a corneal dystrophy. Anyone interested in medico-legal work would like guidance from the meeting. The man was working as a glassblower for thirty-one years without any trouble. Glassblowers do not show any corneal changes; they suffer from lens opacities.

Mr. A. J. B. Goldsmith said that he did not think there was any occupational basis in these cases. Some of his were doing well with weak atropine. In two cases he had scraped the cornea. It meant scraping off rather more than the epithelium, because this opacity was in and underneath

II and III. Retinal Glioma, with Successful Use of Radon Seeds.

In both children the eye with the more extensive growth has been removed and the other successfully treated by the application of radon seeds to the sclera over the growth.

II. Janet C., aged 12.

First attended hospital in November 1939, aged 3 years.

The right eye showed extensive glioma retinae, and was removed. Pathological section of this eye confirmed the nature of the tumour.

In the left eye there were two discrete masses of growth in the mid-periphery at 4.30 and 6 o'clock. Four radon seeds, each of 1.5 millicurie, were stitched to the sclera over the affected areas of the retina and left in situ for six days. Subsequent observation has shown satisfactory shrinkage of the growth and replacement by calcareous deposits. The visual acuity in this eye is now 6/24.

III. Diana P., aged 6.

First attended hospital in October 1942.

The right eye showed extensive glioma retinae and was removed. Pathological section of this eye confirmed the nature of the tumour.

In the left eye there were three discrete foci of growth, in the periphery at 3 and 6 o'clock and nasal to the disc at 10 o'clock. Six radon seeds, each of 1.5 millicurie, were stitched to the sclera over the affected areas of the retina and left in situ for five days. Periodic examination has shown satisfactory shrinkage of the growth. The vision of the eye is now 6/18, slight post-cortical irradiation cataract changes are present.

A younger sister of this child was brought to hospital in 1944 with a glioma in the right eye, which was removed. Fortunately no growth has so far appeared in the left eye.

In 1946 the mother of these two children attended hospital with a letter from her doctor to say that she was again pregnant and that he felt, in view of the history of glioma retinae in her two children, this pregnancy should be terminated. She was sent to a gynaecologist who in turn referred her to a psychiatrist. The psychiatrist agreed that the psychological strain on the mother was sufficient to justify termination of the pregnancy, which was carried out.

In reply to Mr. Seymour Philips, Mr. King said he had been guided by Sir Stanford Cade in regard to dosage of radon. The seeds had a stitch fixed to each end, which facilitated their attachment to the sclera.

IV and V. Two Cases of Myotonic Cataract.

The President said that during the war he had seen at a mental hospital a number of cases of myotonia dystrophica, but cataracts were not very frequent. He did not know whether they came late or appeared only in a certain proportion of cases.

VI. Syphilitic Uveitis.

VII. Foreign Bodies in Both Eyes (shown by H. H. SKEOCH, F.R.C.S.).

F. W., aged 33.

This man has been a diabetic under treatment for twenty years. He states that his eyes were injured in an air-raid in 1940 at Weybridge. Attended hospital on 5.9.47 complaining of, first blurring and later loss of vision in the left eye in the one day. Examination showed right vision to be 6/12, improved to 6/9 with myopic astigmatic correction. Left vision was less than 6/60 (H.M.). The right eye showed an extensive corneal scar (approx. 10 mm. long, obliquely across the upper part of the cornea). The healed corneal scar contained many fragments of debris, metallic and whitish pieces that looked like concrete or plaster. Scattered over the front of the iris and on the anterior lens capsule there were innumerable pieces of whitish material, similar to those in the cornea. Posterior synechia from 5 to 7 o'clock attached the pupillary margin to the anterior lens capsule, on which there was also some exudate. These multiple foreign bodies, both large and small, seemed to be causing no irritation or reaction in the iris tissues of this eye, but one or two large fragments in the angle of the anterior chamber at 6 o'clock were enclosed in endothelium. There was no

[January 8, 1948]

The Capsular Complications of Cataract Extraction

By CHARLES GOULDEN, O.B.E., F.R.C.S.

ABSTRACT.—The author considered the following important points:

- (1) Anterior capsular synechia to a corneal incision (made by a keratome) after the evacuation of a traumatic cataract. This might be detached early by the use of a blunt-ended knife following a perforation of the cornea with a sharp-pointed knife, much like a tenotome.
- (2) The involuntary prolapse of capsule with a cataract incision.
 - (a) The danger of this was demonstrated as the cause of glaucoma, especially if it be found necessary to divide opaque capsular membrane after the extraction.
 - (b) The danger of sympathetic ophthalmia.
- Prolapse might be prevented:
 - (a) By intracapsular extraction.
 - (b) By extracting the lens through an intact pupil, after the use of capsule forceps, followed either by a partial or total iridectomy.
- (3) The treatment of opaque after-cataract.

Various types of opaque capsule membrane were described.

 - (a) Opaque lens fibres imprisoned between anterior and posterior remains of capsule.
 - (b) Grey membrane made of new lens fibres from proliferating subcapsular cells.
 - (c) Elschnig's cells.
 - (d) Much thickened capsular membrane following an extensive hæmorrhage into the anterior chamber occurring about the fifth day after extraction.
 - (e) A thick membrane formed of fibrous tissue following the invasion of the coloboma of the iris after infection at the time of operation. The fibrous tissue comes from the undersurface of the conjunctival flap and causes an updrawn coloboma which is also made narrower by its contraction.

When performing a capsulotomy thickened bands should be avoided and an incision made in thin capsule, *parallel* to thick bands.

If the membrane is very thick and shows signs of being torn from its peripheral attachment when a single needle is used, then

- (1) Two needles may be used after the method of Bowman;
- (2) A Wheeler operation may be performed (Wheeler, 1939, *Collected Papers*, New York, 197);
- (3) Thick capsule may be divided by means of a Ziegler knife, as described by the author, but not in the manner described by Ziegler.

The danger of performing a capsulotomy in the presence of soft lens matter was pointed out.

The occasional occurrence of localized vitreous opacification at the site of a capsulotomy, even in the absence of iridocyclitis, was mentioned.

RÉSUMÉ.—L'auteur considère les complications importantes suivantes:

(1) Synéchie antérieure entre la capsule et l'incision cornéenne (faite avec un kératome après extraction d'une cataracte traumatique. On pourrait la détacher précocement à l'aide d'un couteau à pointe émoussée après perforation de la cornée par un couteau pointu semblable à un ténotome.

(2) Prolapsus accidentel de la capsule au moment d'une incision pour la cataracte.

(a) Le danger de cette complication comme cause de glaucome est démontré, surtout s'il se trouve nécessaire d'inciser une membrane capsulaire opaque après l'extraction.

(b) Le danger d'une ophtalmie sympathique.

Ce prolapsus pourrait être évité:

(a) Par l'extraction intracapsulaire.

(b) Par l'extraction du cristallin à travers la pupille intacte, après emploi de la pince à capsule, suivie d'une iridectomie partielle ou totale.

(3) Traitement de la cataracte secondaire.

Description de diverses formes de membrane capsulaire opaque:

(a) Fibres cristalliniennes coincées entre les restes antérieurs et postérieurs de la capsule.

(b) Membrane grise formée par de nouvelles fibres cristalliniennes provenant de cellules souscapsulaires proliférantes.

(c) Cellules d'Elschnig.

(d) Membrane capsulaire très épaissie suivant une grande hémorragie dans la chambre antérieure vers le cinquième jour après l'extraction.

(e) Membrane épaisse consistant de tissu fibreux, comme suite de l'invasion du colobome de l'iris après infection au cours de l'opération. Ce tissu fibreux vient de la surface inférieure du lambeau conjonctival et produit un colobome soulevé et rendu plus étroit par la contraction.

En faisant une capsulotomie il faut éviter les bandes épaissies et faire l'incision parallèle à ces bandes, dans une partie mince de la capsule.

Quand la membrane est très épaisse et semble être sur le point d'être arrachée de son point d'attache périphérique si on emploie une seule aiguille on peut:

(1) Se servir de deux aiguilles d'après la méthode de Bowman;

(2) Pratiquer l'opération de Wheeler (1939, *Collected Papers*, New York, 197);

(3) Sectionner la capsule par une méthode décrite par l'auteur, employant un couteau de Ziegler, mais pas de la même manière que Ziegler.

Bowman's membrane. Simple swabbing was useless; one had to peel off the superficial layers of cornea—they peeled off like the skin of an onion. Vision had been very much improved by this procedure. The operation was a partial superficial keratectomy.

The President said that if these corneæ were scraped they did fairly well; the condition did not tend to recur.

White Ring.—J. D. M. CARDELL, F.R.C.S.

First described by Coats in 1912, this is a condition which is probably more frequently present than described. The ring is small and, causing no symptoms, may be easily overlooked. The ætiology has been a matter of discussion for many years. Coats and Mayou considered it to be congenital, Ballantyne favoured intra-ocular disease, while others say it is due to superficial trauma.

The case shown probably falls into the last category. The man is an engine-driver, aged 63, who has had several "sparks" in the left eye. The picture differs in no way from the classical—a complete ring of dead-white, roughly circular, dots having a diameter of under 1 mm. at the level of Bowman's membrane.

Sarcoidosis of the Orbit, with Nodular Infiltration and Proptosis, Treated with Injections of

Chaulmoogra Oil.—HELEN DIMSDALE, M.D., M.R.C.P., for S. P. MEADOWS, M.D.

F. L., a man aged 52. In January 1946 he noticed puffiness of the eyelids. His general health was good. Past history of three attacks of left-sided pneumonia, the last attack twenty years ago.

On examination (February 1946).—Fundi, pupils, and external ocular movements normal. Hypertrophy, increased vascularity, and chemosis of the conjunctivæ, bilateral proptosis, left more than right, multiple hard nodular swellings in both lower lids. Enlargement of lacrimal, right parotid, pre-auricular, tonsillar and axillary glands. Liver and spleen not palpable.

Investigations.—Blood W.R. negative. Sedimentation rate 34 mm. in one hour. Blood-count: R.B.C. 5,400,000; Hb. 90%; W.B.C. 14,600 with normal differential. Plasma protein 7.3 gramme/100 c.c.; plasma albumin 3.8 gramme/100 c.c.; Mantoux 1/100 old tuberculin: very weak positive. X-rays: Hands and feet normal; chest—residual fibrosis. Biopsy of orbital nodule: Focal lymphocytic infiltration, epithelial histiocytes, and a multinuclear giant cell.

Progress.—He was treated with generalized U.V.L., but there was a gradual increase in size of the swellings, with tenseness of the orbital tissues, and severe conjunctival injection.

In July 1946 treatment with chaulmoogra oil was started. He was given 2 c.c. (3% solution) intramuscularly once a week for four months. The swellings softened and gradually receded.

In January 1947 he developed an acute left iritis which recovered in three months.

Present condition.—Well; has gained 2 stones in weight. Small nodule left lower lid; left lacrimal gland, and cervical lymph gland on the right side just palpable. Left eye old K.P.

REFERENCE

LOMHOLT, SVEN D. (1934) *Derm. Z.*, 70, 57.

Dr. Dimsdale, in reply to a question, said that chaulmoogra oil was used by Lomholt in 1934 for subcutaneous nodules. Recently the view had been taken that the improvement was spontaneous, as patients treated with tuberculin and other remedies had also recovered.

The following cases were also shown:

Two Cases of Keratitis.—G. FENWICK, F.R.C.S.Ed. (for HAROLD RIDLEY, F.R.C.S.).

Retinal Perivasculitis Treated with Penicillin.—H. E. HOBBS, F.R.C.S.

- г) Сильно утолщенная капсулярная оболочка, которая являлась следствием экстенсивного кровотечения в переднюю камеру и которая встречалась на пятый день после экстракции.
- д) Толстая оболочка из фиброзной ткани, которая являлась следствием вторжения колобомы радужной оболочки после инфекции во время операции. Фиброзная ткань происходит от нижней поверхности конъюнктивального локута и приводит вынутую вверх колобому, которая суживается от сокращения.

При капсулотомии нужно избегать утолщенные связки и разрез сделанный в капсуле должен быть параллельным к утолщенным связкам.

Когда оболочка очень толста и когда имеются признаки ее разрыва от периферального прикрепления при употреблении только одной иглы, можно—

- или 1) употреблять две иглы по способу Бомана;
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Автор также отмечает, что изредка появляется местная непрозрачность стекловидного тела на месте капсулотомии, даже если и нет приодонциклита.

Capsular complications following cataract extraction have become rarer owing to improved technique in operating. They will become still rarer as time goes on and intracapsular extraction becomes better known and more widely practised; nevertheless, capsular complications will continue to arise. Many complications of cataract extraction are due to bad operating, but some capsular complications occur in the practice of the most skilful operators and follow an apparently perfect operation.

In this paper I refer almost exclusively to the operation in which the lens is removed from its capsule, an operation that leaves within the eye the greater part of the lens capsule.

Two types of incision are commonly used: one, in the cornea, and the other an incision at the limbus with the formation of a conjunctival flap, and there are certain advantages and disadvantages that attend each method.

If the incision is corneal, the retraction of the divided tissue is most marked at the anterior and posterior surfaces so that when the edges of the wound come together it is the central part, corresponding to the substantia propria, that meets, leaving a wedge-shaped gap anteriorly and posteriorly. The coagulum which is formed causes the edges of the wound to become adherent one to the other. The anterior wedge-shaped gap becomes filled with epithelium and the posterior gap with endothelium from the cells which line the membrane of Descemet. The cicatricial tissue that forms comes from the corneal corpuscles. As the scar develops it extends upwards into the anterior wedge-shaped area and gradually replaces the plug of epithelium that filled the anterior part of the wound, and in a similar way the posterior wedge-shaped area is filled by scar tissue and the endothelial plug replaced.

When the incision is through the limbus, with the formation of a conjunctival flap, there is a similar retraction of corneal-scleral tissue to that which occurs when the incision is corneal as described above, but in this case the anterior area is not filled with corneal epithelium, but by subconjunctival tissue derived from the deep surface of the conjunctival flap.

Corneal wounds have been found filled after twenty-four hours and experimental investigation of the healing of conjunctival wounds shows that the epithelium over the wound is complete in one hundred and twenty hours. Keratome incisions of the cornea are notorious for the rapidity and ease with which they heal; such incisions are very oblique and delicate, but an incision with a Graefe knife can be at right angles to the surface of the cornea and does not heal as rapidly, and as a result epithelium may line the wound and pass into the anterior chamber and indeed completely line it. A similar thing may occur if a closed corneal wound is reopened during the healing process. The result will be a secondary glaucoma and loss of the eye sooner or later. I have had an example of glaucoma that could not be relieved occurring within six weeks of the extraction.

If there is delayed agglutination of the wound at the limbus when a conjunctival flap has been formed then subconjunctival tissue extends between the two sides of the wound and it may produce a vascularized fibrous membrane which fills the coloboma and becomes continuous with the capsular remains. Again, when an intractable iridocyclitis has followed an extraction, there is frequently found imperfect closure posteriorly of the lips of the limbal incision due to an entanglement of the lens capsule. This is not merely due to the presence

L'auteur montre le danger d'une capsulotomie en présence de matière cristallinienne molle. Il parle de la formation, dans quelques cas, d'opacifications locales du vitreux à l'endroit d'une capsulotomie, même s'il n'y a pas d'iridocyclite.

EXTRACTO.—El autor considera los siguientes puntos importantes:

(1) Sinequia capsular anterior a una incisión corneal hecha con un querotomo, siguiendo a la evacuación de una catarata traumática. Puede ser despegada precozmente usando un cuchillo de punta roma, después de perforar la córnea con un bisturí afilado, de forma parecida a un tenotomo.

(2) Prolapso involuntario de la cápsula en la incisión operatoria.

(a) El peligro del prolapso está en que ha demostrado ser una de las causas de glaucoma, especialmente si ha sido necesario dividir la membrana capsular opaca después de la extracción.

(b) Peligro de una oftalmía simpática.

El prolapso puede prevenirse:

(a) Mediante extracción intracapsular.

(b) Realizando la extracción del cristalino a través de una pupila intacta, previa fijación de la cápsula con pinzas, seguido de iridectomía parcial o total.

(3) Tratamiento de la opacidad post-operatoria.

Se han descrito varios tipos de opacidad de la membrana capsular:

(a) Fibras opacas del cristalino aprisionadas entre los restos anteriores y posteriores de la cápsula.

(b) Membrana gris integrada por fibras cristalinas neoformadas por proliferación de células subcapsulares.

(c) Células de Elschnig.

(d) Engrosamiento de la membrana capsular a consecuencia de una extensa hemorragia en la cámara anterior, sobrevenida aproximadamente al quinto día de la extracción.

(e) Formación de una gruesa membrana de tejido fibroso siguiendo a la invasión de un coloboma del iris por infección durante la intervención. Este tejido fibroso procede de la cara interna del repliegue conjuntival y da lugar a un coloboma vertical, que se hace todavía mas estrecho al contraerse.

Al realizar una capsulotomía deben evitarse las zonas de engrosamiento, y la incisión, hecha sobre zona capsular no engrosada, deberá ser *paralela* a aquellas. Si la membrana es muy gruesa y muestra señales de despegarse de su inserción periférica cuando se usa una sola aguja, puede procederse como sigue:

(1) Pueden usarse dos agujas después del procedimiento de Bowman;

(2) Llevar a cabo la operación de Wheeler (1939, Collected Papers, New York, 197);

(3) Método descrito por el autor, el cual divide el engrosamiento capsular con el chuchillo de Ziegler, pero no con la técnica que describió Ziegler.

Se pone también de relieve el peligro que conlleva realizar una capsulotomía en casos de cristalino blando.

Se menciona asimismo la posibilidad de opacificación localizada del humor vítreo en el punto de la capsulotomía, contingencia que ocurre ocasionalmente, aun en ausencia de iridociclitis.

КАПСЮЛЯРНЫЕ ОСЛОЖНЕНИЯ ПРИ ЭКСТРАКЦИИ КАТАРАКТА

Лекция прочитанная доктором Гуден

КОНСПЕКТ.—Автор приводит следующие важные факторы:

1. Образование передней капсулярной синехии при корнеальном надрезе (кератомом) после эвакуации травматического катаракта. Синехии могут быть отделены заблаговременно при помощи тупого ножа после перфорации роговой оболочки острым ножом, на подобие тенотома.

2. Непроизвольный пролапс капсулы при надрезе катаракта:

а) Это явление было приведено как причина глаукомы, в особенности когда необходимо перерезывать непрозрачную капсулярную оболочку после экстракции.

б) Риск симпатической офтальмии.

Пролапс может быть предупрежден:

а) Путем интракапсулярной экстракции.

б) Путем извлечения хрусталика через нетронутый зрачок при помощи капсулярных щипцов с последовательной частичной или полной придектонией.

3. Обсуждено лечение последствий непрозрачного катаракта и описаны разные типы непрозрачной капсулярной оболочки:

а) Непрозрачные волокна хрусталика заточенные между передними и задними остатками капсулы.

б) Серая оболочка сформированная из новых волокон хрусталика от отрывков субкапсулярных клеток.

в) Клетки Эллинга.

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of a piece of capsule acting as a foreign body in the wound; the piece of capsule must still be attached to the ciliary body. Incidentally, such eyes are extremely dangerous from the point of view of sympathetic iridocyclitis. Very similar results follow the prolapse of vitreous, a strand of which may be left imprisoned in the operation wound.

It is not suggested that capsule imprisoned in the operation scar always leads to disaster, but at one time there were innumerable irritable red eyes following extraction. Many cases showed a strand of lens capsule passing through the coloboma to the operation scar and it was only when this was appreciated and great care taken to be certain that all lens capsule was returned to the eye that the number of irritable eyes was reduced and posterior capsulotomy became a safe operation, free from anxiety. It took many years to convince ophthalmic surgeons how important it was to be certain that the operation scar was free from imprisoned capsule. This gospel was preached incessantly by William Lang but it took a long time to find the remedy for a complication that might happen to an apparently perfect operation performed by a highly skilful operator. Mr. Morton, an extraordinarily beautiful operator, used, in all cases of cataract extraction, to deliver the lens through a complete and undilated pupil, and in this he was followed by Devereux Marshall. A large proportion of cases were left as simple extractions and those that did not prolapse subsequently gave the best results of all cases of extraction that were done at Moorfields when, as Senior House Surgeon, I had charge of the cataract wards. Here then was the remedy to prevent the unwitting leaving of "capsule in the wound". If the lens were delivered through an intact pupil and care was taken that the iris was perfectly returned to the eye then it was certain that all lens capsule was returned to the eye and it mattered not, so far as the capsule was concerned, whether an iridectomy was performed or not.

The serious complication is, of course, prolapse of the iris, which occurs during the first ten hours after the cataract operation. We knew that, because Morton gave instructions that the cases on which he had operated, between 10 and 11 o'clock in the morning, were to be inspected the same evening, and any prolapsed iris was to be removed there and then. We usually inspected the cases about 5.30 and if prolapse had not occurred then, we looked upon the eye as safe. At the time of the extraction only cases that were apparently unlikely to prolapse were left with an intact pupil; so such cases were picked. In spite of that, prolapse of the iris was common and we were very much bored by having to operate at that time of day when many new cases were waiting for their case-sheets to be made out. Most surgeons look upon prolapsed iris after extraction as a serious matter.

METHODS OF OPERATION THAT MODIFY AFTER-CATARACT

After-cataract does not follow an intracapsular extraction which has been successfully performed.

The use of capsule forceps when the lens is extracted from its capsule membrane certainly does leave a much thinner capsular membrane, sometimes merely a crinkled posterior capsule in the pupillary area, and often one that is transparent and smooth.

There is one condition in which capsule forceps are essential, and that is those cases in which the anterior capsule of lens has become dotted. If the anterior capsule is not removed in such cases a subsequent needling may fail to give a clear gap, as the dotted capsule will remain in the middle of the pupillary area in spite of being temporarily pushed aside by the discission needle.

I do not know if capsule forceps are in common use. English models are usually very clumsy, with large rough teeth, but those made by Greishaber from Vogt's specification are beautiful. Attempts have been made to copy them in London, but they are comparatively gross.

There is much to be said for early needling and Herbert in India operated ten days after extraction. This seems very early, but in India unless the needling were done before the patient left hospital there was no other chance owing to the distance from which patients came. In England the needling may be done a month after the patient has returned home, that is six weeks or so after the extraction. The posterior capsule is still elastic and will gape when an incision is made in it; if, however, we wait until it has become opaque and degenerated, then it becomes like a piece of cigarette paper and will not gape when incised. Bowman first pointed out the elasticity of the lens capsule and the accommodation hypothesis of Fincham depends on this feature.

THE RELATION BETWEEN CAPSULE ADHERENT TO THE OPERATION SCAR AND GLAUCOMA

This relation was thoroughly and extensively investigated by Natanson, who published his results in 1889, and Treacher Collins in 1890.

It has already been noted that glaucoma following a cataract extraction may be due to corneal epithelium invading the anterior chamber and subsequently lining it, and this is more likely to occur when the incision is corneal.

When the incision is at the limbus with the formation of a conjunctival flap the lens capsule may become adherent to the operation scar, as also it may be adherent to a corneal section. In those cases that develop glaucoma, the angle of the anterior chamber was closed by the adhesion of the root of the iris to the posterior surface of the cornea, and in all these eyes there was an adhesion of the lens capsule to the operation scar. In some cases, in spite of the adhesion of the lens capsule to the scar, glaucoma did not arise until a needling operation was performed, so that if an adherent capsule does not produce glaucoma, at any rate it predisposes to glaucoma by a shallowing of the anterior chamber.

ANTERIOR SYNECHIA AFTER A LINEAR EXTRACTION OF A SOFT CATARACT OR AFTER EVACUATING A TRAUMATIC CATARACT

(1) This is less frequently seen since anterior chamber washout became more usual.

(2) Lang's incision in the upper part of the cornea was the result of his experiment with Fukala's operation for high myopia. He did 80 cases before he abandoned the operation largely because of the frequency of detachment of the retina. This was one of the early observations of the connexion between dissection of a lens and detached retina. It is now appreciated how often detachment of the retina occurs years after an operation for, say, zonular cataract. Lang introduced the operation of "curette evacuation" through an incision in the upper part of the cornea, because if an adherent or prolapsed capsule followed, he was able with Lang's twin knives to separate capsule that was adherent to, or prolapsed through, the cornea. Previous to the adoption of this plan of operation, lens matter was commonly let out by incision at the limbus down and out. The reason for choosing this site was that during an imperfect anæsthesia with chloroform, the eyes turned upwards and this was the site most easily available for incision. It needed great skill on the part of the anæsthetist to arrange that the depth of anæsthesia was such that the eye turned downwards allowing the upper part of the cornea to be available for operation. As the result of making an incision down and out at the limbus, the capsule not infrequently prolapsed, and also the iris. This was very difficult to deal with and, in the case of prolapsed capsule, impossible. Many bad results from operation for zonular cataract are due to these accidents. By placing the incision in the upper part of the cornea half-way between the margin of the cornea and the centre, it becomes possible to divide this synechia by means of the twin knives. If, however, the prolapse of capsule occurred at the periphery, especially down and out, then it was impossible to divide the synechia, and the eye was left for ever with a capsule synechia which, even if the eye settled down, was in danger of subsequent glaucoma, especially if a dissection of capsular membrane became necessary later on.

OPAQUE CAPSULAR MEMBRANE

There are several types of opaque capsular membranes, usually called "after-cataract":

(1) That in which the anterior and posterior portions of the lens capsule become more or less agglutinated, imprisoning soft cortical lens matter.

(2) An opaque membrane due to the proliferation of anterior capsule cells forming greyish lens fibres as a sheet filling the pupillary area.

(3) Elschnig's cells due to a globular degeneration of new lens fibres usually attached to a posterior iris synechia.

(4) A modified and much thickened capsule, with a felted surface following an extensive hæmorrhage into the anterior chamber about one hundred and twenty hours after the extraction.

It is remarkable that blood that remains in the anterior chamber immediately following the extraction disappears very rapidly, but the blood that appears about the fifth day takes, sometimes, several weeks to disappear.

This blood, I think, always comes from the conjunctival flap, possibly from the vessels that have invaded the limbal incision. I have watched the hæmorrhage occur, and it falls downwards through the anterior chamber in a worm-like way.

(5) A thick membrane formed of fibrous tissue which follows the invasion of the coloboma of the iris after infection at the time of operation. The fibrous tissue comes from the under-surface of the conjunctival flap and causes an up-drawn coloboma which is also made narrower by its contraction.

Very little investigation has been made on the composition of capsular membranes. One was published in 1900 by W. H. Bates, who is now better known in connexion with a method of treatment to which his name is attached.

of a piece of capsule acting as a foreign body in the wound; the piece of capsule must still be attached to the ciliary body. Incidentally, such eyes are extremely dangerous from the point of view of sympathetic iridocyclitis. Very similar results follow the prolapse of vitreous, a strand of which may be left imprisoned in the operation wound.

It is not suggested that capsule imprisoned in the operation scar always leads to disaster, but at one time there were innumerable irritable red eyes following extraction. Many cases showed a strand of lens capsule passing through the coloboma to the operation scar and it was only when this was appreciated and great care taken to be certain that all lens capsule was returned to the eye that the number of irritable eyes was reduced and posterior capsulotomy became a safe operation, free from anxiety. It took many years to convince ophthalmic surgeons how important it was to be certain that the operation scar was free from imprisoned capsule. This gospel was preached incessantly by William Lang but it took a long time to find the remedy for a complication that might happen to an apparently perfect operation performed by a highly skilful operator. Mr. Morton, an extraordinarily beautiful operator, used, in all cases of cataract extraction, to deliver the lens through a complete and undilated pupil, and in this he was followed by Devereux Marshall. A large proportion of cases were left as simple extractions and those that did not prolapse subsequently gave the best results of all cases of extraction that were done at Moorfields when, as Senior House Surgeon, I had charge of the cataract wards. Here then was the remedy to prevent the unwitting leaving of "capsule in the wound". If the lens were delivered through an intact pupil and care was taken that the iris was perfectly returned to the eye then it was certain that all lens capsule was returned to the eye and it mattered not, so far as the capsule was concerned, whether an iridectomy were performed or not.

The serious complication is, of course, prolapse of the iris, which occurs during the first ten hours after the cataract operation. We knew that, because Morton gave instructions that the cases on which he had operated, between 10 and 11 o'clock in the morning, were to be inspected the same evening, and any prolapsed iris was to be removed there and then. We usually inspected the cases about 5.30 and if prolapse had not occurred then, we looked upon the eye as safe. At the time of the extraction only cases that were apparently unlikely to prolapse were left with an intact pupil; so such cases were picked. In spite of that, prolapse of the iris was common and we were very much bored by having to operate at that time of day when many new cases were waiting for their case-sheets to be made out. Most surgeons look upon prolapsed iris after extraction as a serious matter.

METHODS OF OPERATION THAT MODIFY AFTER-CATARACT

After-cataract does not follow an intracapsular extraction which has been successfully performed.

The use of capsule forceps when the lens is extracted from its capsule membrane certainly does leave a much thinner capsular membrane, sometimes merely a crinkled posterior capsule in the pupillary area, and often one that is transparent and smooth.

There is one condition in which capsule forceps are essential, and that is those cases in which the anterior capsule of lens has become dotted. If the anterior capsule is not removed in such cases a subsequent needling may fail to give a clear gap, as the dotted capsule will remain in the middle of the pupillary area in spite of being temporarily pushed aside by the dissection needle.

I do not know if capsule forceps are in common use. English models are usually very clumsy, with large rough teeth, but those made by Greishaber from Vogt's specification are beautiful. Attempts have been made to copy them in London, but they are comparatively gross.

There is much to be said for early needling and Herbert in India operated ten days after extraction. This seems very early, but in India unless the needling were done before the patient left hospital there was no other chance owing to the distance from which patients came. In England the needling may be done a month after the patient has returned home, that is six weeks or so after the extraction. The posterior capsule is still elastic and will gape when an incision is made in it; if, however, we wait until it has become opaque and degenerated, then it becomes like a piece of cigarette paper and will not gape when incised. Bowman first pointed out the elasticity of the lens capsule and the accommodation hypothesis of Fincham depends on this feature.

THE RELATION BETWEEN CAPSULE ADHERENT TO THE OPERATION SCAR AND GLAUCOMA

This relation was thoroughly and extensively investigated by Natanson, who published his results in 1889, and Treacher Collins in 1890.

It has already been noted that glaucoma following a cataract extraction may be due to corneal epithelium invading the anterior chamber and subsequently lining it, and this is more likely to occur when the incision is corneal.

The instrument is a Graefe knife with a blade 18 mm. long and 1 mm. wide.

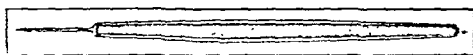


FIG. 2.—Discission knife for after-cataract. Blade is 18 mm. long and 1 mm. wide.

The surgeon stands at the head of the table and a little to the left of the eye to be operated on. A speculum is introduced and the eye is fixed by grasping the conjunctiva and subconjunctival tissue below the cornea at a point diametrically opposed to the point where the knife is to enter the cornea. The fixation forceps is held in the left hand without the slightest pressure on the eyeball.

The handle of the knife is taken most delicately between the pulps of the forefinger and thumb 2 inches (50 mm.) from the point of the knife, and care is taken that there is no tendency of the finger to wrap itself round the handle. This would render the execution of the technique impossible.

The eye looks slightly downwards, and the point enters the upper part of the cornea 1 mm. from this limbus, in front of the coloboma (when an iridectomy has been made at the time of the lens extraction). The incision is planned to go through the heaviest bands if possible, but the bands can be cut at any angle; and it is well to carry the incision into the coloboma.

The knife point is carried deliberately across the anterior chamber and behind the inferior portion of the iris, and carefully brought in contact with the capsular membrane. One can take all the time one wants in this part of the procedure, provided the fixation forceps and the knife are held in absolute relaxation. The rest of the operation is done speedily so that the incision is completed before the capsular membrane begins to relax from division. By an absolutely simple movement on the part of the surgeon the point and cutting edge of the knife blade are put through just the sort of excursion that is needed to produce a long-drawn incision in the membrane without enlargement of the surface wound in the cornea.

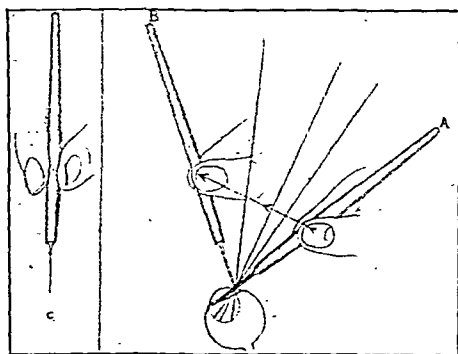


FIG. 3.—Mechanics of discission. Finger and thumb hold knife lightly, and are carried along arrowed line. Knife point courses in vitreous body along dotted line. C gives view of back of knife as held in fingers.

(Figs. 2 and 3 are reproduced from "Secondary Cataract Opening by Single Straight Incision" by John M. Wheeler, *Trans. Amer. Acad. Ophthalm. Oto-Laryng.*, 1924, p. 149.)

From the position in which the knife is held with the point in gentle contact with the capsular membrane, the part of the knife handle between the pulps of the finger and thumb is carried in a straight line by a free rapid movement of the arm, without any change in the position of the hand and wrist. By this movement the blade is made to slip in and out of the vitreous without any interruption in the sliding motion on the membrane, and the non-cutting edge of the blade receives gentle pressure against the cornea until the blade slips out of the corneal wound, usually without loss of aqueous (fig. 3). As the end of the forefinger and thumb are carried along a straight line from position A to position B, the knife handle changes position as though working freely on a pin passing through the knife handle set in the pulps of the forefinger and thumb. This imaginary pin passes straight along the course

THE OPERATIVE TREATMENT OF AFTER-CATARACT

An operation was described by Sir William Bowman on May 24, 1853. He entitled his paper: "On the Use of Two Needles at Once in Certain Operations on the Eye, Especially in Those for Capsular Cataract and Artificial Pupil".

(1) This operation has been recently revived, but I have no personal experience of it. This operation overcomes difficulties met with in thickened capsules and those that tend to become detached at the periphery. When this occurs the surgeon is placed in an impossible position as the mere displacement to one side of the opaque membrane is never permanent, in that it always returns to its original place.

If two needles are brought to bear on the opaque capsule from different sides of the cornea or sclerotic, each furnishes the other with a point of resistance, and the capsule may be torn open or cut at pleasure in almost any direction, and generally without any drag on the neighbouring vascular structures.

A great advantage of this mode of operating is that it may be at once adopted in any case where, on trial, a single needle is found to be insufficient to effect the laceration of the obstructing membrane. It is usually possible to decide before setting out upon an operation whether it may be carried out with one needle only, but on other occasions the needle alone can afford a correct intimation of its texture.

Bowman devised a needle, known as the "stop needle", which is now hard to come by. One uses it now, not because of the stop, but because it is perfectly cylindrical and the cutting portion makes a hole into which the shank exactly fits. It may be remarked here that a needle that has been re-ground is of no value for a discission, as the cutting part has been reduced and no longer makes a perforation that will admit the shank of the needle precisely, so that it jams. This not only bruises the eye, but causes a wrinkling of the cornea which very much interferes with the view the surgeon has of the membrane and the effect of his endeavours to cut it. To avoid the chance of inadvertently penetrating too far with one of the needles, whilst the attention is engaged on the other, the stem of the needles is made thicker from the handle up to within half an inch of the point; in no case is it necessary to enter the instrument beyond half an inch in length.

(2) For a capsular membrane that is not unduly tough or, what is more important, movable or likely to become detached, I personally use a Ziegler needle and preferably one made by Grieshaber of Schaffhausen.

These are made very precisely and the cutting portion makes an incision that just admits the shaft of the needle so that it may be partially withdrawn from the eye or pushed farther into the eye without fear of loss of aqueous.

Furthermore, if it is returned to Grieshaber to resharpen, they slightly reduce the diameter of the shaft so that the cutting portion still makes an incision into which the shaft fits precisely.

I do not use the instrument in the way described by Ziegler who introduced the instrument for the performance of iridotomy in cases in which, after cataract extraction, the iris has become drawn up to the scar of the extraction incision. Choosing a portion of the capsular membrane free from toughened bands I puncture it parallel to the surface of the vitreous and then, pushing on the cutting portion of the needle as much as possible between membrane and vitreous face, I again puncture the membrane and then depress the handle of the instrument so as to raise the capsular membrane forwards and then cut upwards either by a dragging movement or a sawing movement. In that way a triangular piece of the capsular membrane is cut with the base below (fig. 1).

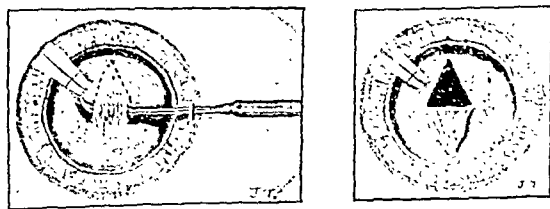


FIG. 1.—Method and result of discission with Ziegler's knife.

Given a good cutting instrument quite tough membrane can be cut.

(3) Wheeler has devised a most useful procedure for dividing a capsular membrane and it is of great value in dealing with tough membranes. Further, it is the best method I know for performing an iridotomy after a removal of the lens.

I was interested by the remarks Mr. Goulden made at the end of his paper in regard to the thickening of the anterior vitreous after capsulotomy. I used to think that once there was a good gap in the capsule it would never close but rather to my dismay not long ago I had one which did close and I had to ask Mr. Goulden about it. He and I thought the eye would never get better vision. However, I tried once more and got a good gap through the apparently opaque layer of vitreous and, in the end, I achieved a definite improvement on my original result.

Professor W. J. B. Riddell: With regard to the position of the stop on the needle, Mr. Goulden would like to have it $\frac{1}{4}$ inch from the point, which is 12.5 mm. Should it not be rather less than $\frac{1}{2}$ inch, because this would take it right across the anterior chamber before the stop would come into action; the diameter of the cornea being about 11.5 mm.?

Mr. H. M. Traquair: Mr. Goulden did not mention the method, used frequently by Marshall, of dividing the capsule with the knife as it passes across the anterior chamber. In Edinburgh about 1910 discission was the common practice, but one gave up the cystitome after the first year or so for the capsule forceps, because it seemed to be a great advantage to be able to remove the whole of the anterior capsule. I would like to give credit to Dr. George Mackay of Edinburgh for the invention of a good pair of capsule forceps which, if properly used, enabled practically the whole of the anterior capsule to be removed so that none, or very little, of the soft lens matter remained, and the need for subsequent needling was very much diminished.

The next step, and one which developed in Edinburgh because we had learned to use the capsule forceps, was the introduction by Sinclair of the intracapsular operation. Edinburgh is strongly in favour of that operation because it is regarded as not only the easiest but the safest method of cataract extraction.

I whole-heartedly support the view that discission is by no means to be given up. The late Sir George Berry advocated discission with two needles by passing them through the membrane and then turning the shanks upwards so as to pull the capsule apart, the advantage of two needles being that traction on the ciliary body was largely, if not altogether, avoided. Latterly, when doing discission I have used two Ziegler needles, introduced and then turned so that the cutting edges point backwards with the points crossing in the middle of the membrane. Then, when the shanks are approximated, there is even less danger of traction as a cutting action is obtained if the needles are sharp.

I have often used Wheeler's knife but it seemed to plunge too deeply into the vitreous. Apart from lamellar cataracts, and so on, my Ziegler's and Wheeler's knives have lain unused for a good many years now. In using Wheeler's knife Mr. Goulden indicated that its point should be directed vertically downwards before turning the handle up. I feel that one needs to be careful to avoid the danger of traction when using a single instrument. The membrane is searched for a thin part and the knife inserted opposite that weak spot so that it can be passed across the anterior chamber to pierce the capsule at that point. There is no fixed rule that the incision should be vertical.

An annoying occasional complication in the old days was an adhesion of the vitreous to the wound causing an opacity like a strand of seaweed which hung down and waved before the patient's sight, creating a great deal of annoyance, and which it was impossible to remove.

Mr. H. B. Stallard: Mr. Goulden has spoken of the danger of strands of vitreous coming into the wound on withdrawing the knife-needle after the capsulotomy. There is an Indian practice whereby, after the knife has made the incision through the capsule, it is passed on to the filtration angle opposite the site of entry, turned round sharply several times and then withdrawn quickly, thus disentangling any strands of vitreous from the point of the knife-needle. The principle is much the same as when withdrawing a spoon from a jar of honey.

Mr. J. G. D. Currie: How much real damage occurs when an incision actually goes rather farther back into the vitreous than we usually do nowadays? I know that the general practice in the past was to cut rather far back into the vitreous when needling, and certainly in Wheeler's operation this is almost bound to be done. The practice is now to pick up the capsule and move anteriorly, but sometimes this gives one very restricted room if the capsule is rather elastic. It has always been a moot point in my mind whether one should cut back or not on these occasions.

Mr. M. H. Whiting: The double needle operation offers great advantages for capsulotomy, but there is no need to use two needles if the capsule is thin and it is desired to operate three or four weeks after the cataract extraction, which is what I prefer to do.

Mr. Goulden referred to opaque vitreous coming up into the capsular opening after capsulotomy. I can only remember one occasion on which that happened and I am certain that in that case it was actually opaque vitreous from cyclitis beforehand, which did not oppose so much obstruction to the light when the surface of the vitreous was flat, but when the little knob of vitreous came forward through the opening in the capsule it was a much greater obstruction. The vision of this particular patient was reduced about two lines instead of being improved. The interesting point was that I watched that patient for some time afterwards and the little knob of vitreous actually flattened down and became level with the surface of the capsule and the vision improved correspondingly until finally I got the vision I anticipated I should get from the capsulotomy.

Mr. B. W. Rycroft: Has any member had experience of examining the lens capsule with ultraviolet radiation? A short time ago I saw a demonstration in a foreign clinic where the Philips' ultraviolet lamp was used. It was very uncanny in a darkened theatre to see the rows of gleaming white teeth surmounted by pairs of mature soft white cataracts. The practical value is that a dislocated lens in the vitreous or a fine strand of capsule is very visible against a dense black background. It

indicated by the arrowed line in the slide, and the knife slides in and then out as it goes across the eye, and the operation is done.

The result of this act is a straight incision which gradually opens up and never has a tendency to close. Manifestly the opening must be in the visual line, but the width is not important as long as it is properly placed. The effect of severing a band is shown by a slight angulation in the edges of the opening where the band is cut. There is no membrane, no matter how heavy the bands, that will not open out freely by this method if the knife and the technique are correct.

In cases in which there is capsule imprisoned in the extraction wound, especially if considerable in amount, there is the risk that glaucoma will occur as a result of capsulotomy. This was especially the case when the discission needle was not used as a cutting, but as a tearing, instrument and in the days when less care was taken to prevent capsule becoming imprisoned in the wound and its danger and significance were not appreciated, and a rough use of a discission needle was common. I have seen the most lamentable results. In fact discission was looked upon as an operation to be avoided if possible. Many surgeons would not touch an eye that had 6/12 of vision and as a house-surgeon one was not expected to admit cases for capsulotomy that had a vision of 6/18.

OPAQUE CAPSULE IN THE PRESENCE OF LENS REMAINS

After an extraction of a senile cataract soft cortex is frequently left behind, sometimes in fair amount, although this is less frequent since the routine wash-out of the anterior chamber. Masses of opaque lens remains become imprisoned between portions of anterior and posterior capsule, but as these are so often behind the iris they are not of importance in this respect. It is rather those lens remains in the pupillary area that are of importance. Patience must be practised and due time allowed for these remains to absorb before a discission is made, because if the posterior capsule be incised in the presence of soft lens remains, trouble will be experienced with a mixture of vitreous and opaque lens matter. If the process of absorption is unduly slow, then the lens matter may be broken up with a needle without perforating the posterior lens capsule and another period allowed to elapse so that the lens material may absorb. It is notable how much frequent and regular hot bathing of the eye will assist this absorption. Then, when all lens has disappeared, the posterior capsule may be divided.

THE PROLAPSE OF VITREOUS INTO THE ANTERIOR CHAMBER AFTER A NEEDLING OPERATION

If vitreous has escaped during a cataract extraction, a thicker or thinner strand becomes imprisoned in the operation scar, and when a vigorous needling has been performed a strand of vitreous follows the withdrawal of the needle and is imprisoned in the needle puncture. In these cases glaucoma may be the result either of the extraction or needling, and a pathological examination will disclose a shallowed anterior chamber and a blocking of the angle much as in those cases in which the capsule of the lens is imprisoned in the extraction scar. Apart from these accidents, vitreous is always prolapsed into the anterior chamber even in the most gentle and best planned needling of the posterior capsule. This prolapse is never extensive when the needling is properly performed, but it may always be seen with the slit-lamp and invariably some small brown particles of uveal dust are found mixed with the greyish flocculent-looking prolapsed vitreous. The prolapsed vitreous I think tends to become less in amount as time goes on. I have never seen vitreous prolapsed in a gross amount into the anterior chamber as a result of needling in a case uncomplicated by the adhesion of capsule to the operation scar.

OPAQUE VITREOUS FOLLOWING CAPSULOTOMY

I have, on a few occasions, seen the vitreous in the immediate district of a capsulotomy become opaque and thus interfere with vision and lead to a disappointing visual result, and this opacity has remained permanent. The flocculent mass of vitreous in the capsular opening may be found if the operation of needling is performed during an attack of cyclitis.

Mr. Harold Ridley: In modern extracapsular cataract extractions the middle of the anterior layer of the lens capsule is generally removed with capsule forceps, instead of being simply incised with a cystitome or the point of the cataract knife. Consequently complications due to a dense capsule is much less frequent and often an acuity of 6/6 is obtained without division of the delicate posterior layer. In his paper Mr. Goulden did not mention how he dealt with dense bands in the capsule but I believe that his policy is not to attempt division of these but to perform the capsulotomy through an adjacent thin area.

Mr. Arthur Lister: I have had the privilege of watching Mr. Goulden do a Wheeler's iridotomy and it is worth seeing the crisis of the operation as he poises with the knife in position and then the blade goes back like lightning through the capsule.

Section of Odontology

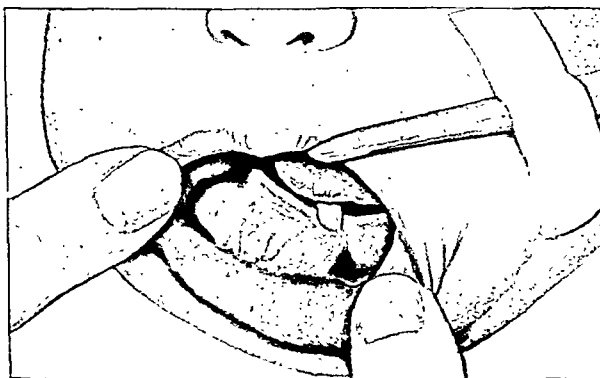
President—HUMPHREY HUMPHREYS, O.B.E., M.C., M.B., F.D.S.

[January 26, 1948]

Melanotic Adamantinoma of the Mandible in a Child Aged 5 Months.—S. H. WASS, M.S., F.R.C.S.

ON August 30, 1947, Dr. Rosenberg of Worthing referred to my Out-patient Department at Guy's Hospital a female child, aged 5 months, with a swelling of the right lower jaw. This swelling had been first noticed six weeks previously and the mother was of the opinion that it had increased rapidly in size during this time. At first the swelling did not appear painful, but more recently it had seemed tender to touch and the child had become fretful though the general health of the child was satisfactory.

On examination there was a visible external swelling in the region of the right lower jaw without any change in the overlying skin. Inspection within the mouth (fig. 1) revealed a



[ARTIST, S. TREADGOLD]

FIG. 1.—Showing swelling of outer table of mandible.



FIG. 2.—Intra-oral radiograph showing expansion and thinning of outer table of mandible with translucent zone apparently containing temporary canine tooth.

smooth, ovoid swelling of the outer table of the right side of the mandible in the 5-1 region. The lower border and alveolar margin of the jaw were not involved and there was no expansion of the inner table. The right lower central incisor (temporary) was the only tooth erupted. The swelling was firm in consistency, well defined at its edges and had a smooth surface. It was not tender and there was no fever. The soft tissues of the cheek were normal and there was no enlargement of the cervical glands.

The intra-oral radiograph (fig. 2) showed expansion of the outer plate of the mandible in

is possible to get this lamp in England, and I feel it has a practical application in a small group of cases.

The President: The Grieshaber capsule forceps is certainly a beautiful instrument and works exceedingly well for the extracapsular operation.

I should like to ask Mr. Goulden whether, in the case of capsular strands remaining after extraction, it is not at least as important as the attachment back to the ciliary body that these strands should not reach the surface between the lips of the wound, because in such a case a track would exist along which infection could reach the interior of the eye from the surface.

Mr. Charles Goulden: I do not think I know what the mechanism of the consequence of capsule in the wound is, why it should keep an eye irritable. I had not looked upon it as being infective. Does anybody know the reason why an eye should remain so irritable with capsule attached to the ciliary body? Is it infective?

Mr. E. Wolff: Does it not leave the way permanently open? So long as there is capsule in the wound and there is no proper healing, infection can, in time, travel down the wound.

Mr. Goulden: In answer to Mr. Ridley: I think it important that any incision made in the capsule remaining after extraction should be through thin membrane and parallel to thickened bands. No attempt should be made to cut thickened bands.

Dealing with Professor Riddell's point, let me say that I copied the description of Bowman's needle from his original paper, in which the thinner part of the needle from the point to the thicker part is described as $\frac{1}{2}$ inch long.

Mr. Traquair spoke of the anterior dipping of the knife in the operation of extraction, so as to perforate the anterior lens capsule. I first saw it done by Morton and Marshall and I think it a mistake. The pioneer in England of the use of capsule forceps was John Couper. Mr. Traquair mentioned Dr. Mackay.

Mr. Traquair: In Edinburgh!

Mr. Goulden: I do not know who was the first in the field, Couper or Mackay. I think Couper's forceps of great use in dealing with prolapsed iris after an accident. For the purpose for which they were invented they are coarse and clumsy and not to be compared with Vogt's capsule forceps made by Grieshaber.

I agree with what has been said in regard to intracapsular extraction, which I think, without doubt, is going to be the operation of choice.

I am much obliged by Mr. Whiting giving us the benefit of his experience. I understand he used the double needle only when dealing with difficult cases.

Then Mr. Currie spoke of the question of the depth to which one should dip the needle. On general principles it seems to me one should disturb the vitreous as little as possible. Hence the method of sliding the needle between the capsule and the face of the vitreous. I would not say more than that. The vitreous is not often dislocated very much into the anterior chamber, even when the needle is roughly used.

In the presence of a tough capsule, with the ordinary operation with a needle, you are between the devil and the deep blue sea! If you try to needle the capsule in the ordinary way it is impossible, and you will partially dislocate the capsule and leave no gap. The double needle operation may be used, but of that I have no experience. The use of Wheeler's operation disturbs the vitreous very little.

Mr. Currie: That is what I was interested in, that it did seem to disturb the vitreous so little.

Mr. Goulden: In reply to Mr. Rycroft, the only experience I have had as to the use of ultraviolet radiation was when I saw Kalt in Paris, at the age of 78, performing intracapsular extractions. He demonstrated, if the lens became dislocated into the vitreous, that with ultraviolet light the lens was easily seen. I have never, apart from this occasion, seen anyone of 78 years operating for cataract.

The post-operative course was undisturbed and healing of the mucous membrane took place by first intention. The child was examined again two months after operation (December 1947) when the jaw was firm; radiographs showed complete re-ossification of the mandible. There was no clinical swelling and the child was in good health. The ultimate prognosis with regard to this rare tumour cannot be assessed. A search of the literature reveals only one similar case previously recorded (Mummery and Pitts, 1926). This case was identical in all its features with the one presented to-day and was recorded to have survived four years after operation without any signs of recurrence.

I am indebted to Miss S. Treadgold, of Guy's Hospital, for the water-colour drawing and to Mr. J. E. Hutchinson of the Department of Dental Medicine, Guy's Hospital, for the photomicrographs. My thanks are also due to Professor M. A. Rushton for his help and interest in the diagnosis and treatment of the patient.

REFERENCE

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Electronic Apparatus for Immediate Visual Recording of Pulse Rate. [*Abstract*]

By W. ROTHERAM, M.D.S., M.B., Ch.B.

(*Late Major, Officer Commanding a Surgical Team in the Middle East*)

A SERIES of experiments was outlined, using electronic methods and principles—the object being to devise apparatus which would give a continuous visual recording of pulse rate on a scale marked in beats per minute and applicable during operation upon major surgical cases. The experimental stages were reviewed and the reasons for the adoption of the particular circuit arrangements were explained.

The apparatus was then described in its final form—constructed as one unit—the component parts and individual circuit sections consisting of the following:

- (1) The arrangement for initial pick-up of the impulse.
- (2) An amplifier section.
- (3) A "Limiter" circuit which it was necessary to include to ensure that in spite of variations in volume and amplitude of the pulse, a constant voltage would be "fed" into the succeeding stages of the apparatus.
- (4) A Diode Rectifier—to turn the alternating impulse into a unidirectional one.
- (5) A recording valve—a final stage consisting of a voltage amplifier and milliammeter (with a full-scale deflection of one milliamp).

The electronic principles underlying the properties of a condenser and resistance were described—these being an essential (though small) part of the circuit arrangement. This was in connexion with that section of the apparatus which actually carried out the "count" of the impulses—and in relation to that property of a condenser and resistance known as a "Time-Constant"—this being the time taken for a condenser to charge when associated with a particular resistance.

The panel controls were then described—the most important one consisting of a resistance (variable) included in the Diode circuit (*see* 4)—this variable serving to "open" or "close" the scale of the instrument, e.g. 40 to 180 beats/min. or 70 to 90 beats/min.—several ranges being available by adjustment of this control. The methods used to calibrate the instrument were given.

The method of operation of the instrument was described including the adjustment of the panel controls for the individual case.

Finally the uses of the apparatus were summarized as follows:—

- (1) In prolonged and extensive surgical procedures especially in cases of serious injuries.
- (2) In anaesthesia—particularly of long duration.
- (3) In any other cases where second-to-second observation of pulse rate is important.

the region of the swelling. The bone of the outer table was extremely thin and was absent in one place. Deep to the outer table was a rounded, clear, translucent zone which appeared to contain the temporary canine tooth. On these radiographic findings a provisional pre-operative diagnosis of a dentigerous cyst was made, although the rarity of such a cyst in relation to a deciduous tooth was fully appreciated.

The child was admitted to hospital but owing to intercurrent infection operation was delayed until October 1947. During this period in hospital the swelling of the jaw showed no increase in size and the physical signs remained unaltered. Operation was undertaken under intratracheal anaesthesia by Dr. J. Gordon. After injection of local anaesthetic solution a flap of mucous membrane was raised from the outer side of the mandible over the tumour. The outer surface of the tumour was covered by a thin layer of bone, but in two places the bone of the outer table had completely disappeared and the fibrous capsule of the tumour was visible. The thin bone was removed from the surface of the tumour and the unerupted deciduous canine and lateral incisor teeth were found to have been pushed outwards by the tumour and not to be contained within it as the radiographs had suggested. The tumour was encapsulated and shelled out easily from the mandible. At the conclusion of the operation the mucous membrane flap was sewn back in position.

The tumour removed from the jaw was solid, ovoid in shape and measured 2 cm. by 1.5 cm. The cut surface was firm, white in colour, and showed a large patch of bluish-black pigmentation. I am indebted to Dr. S. de Nevasquez for the following pathological report:

"The specimen is a smooth solid oval tumour 2 by 1.5 cm. of uniformly firm consistency, the cut surface of which is mottled by flecks of black pigment. Microscopically the tumour consists of

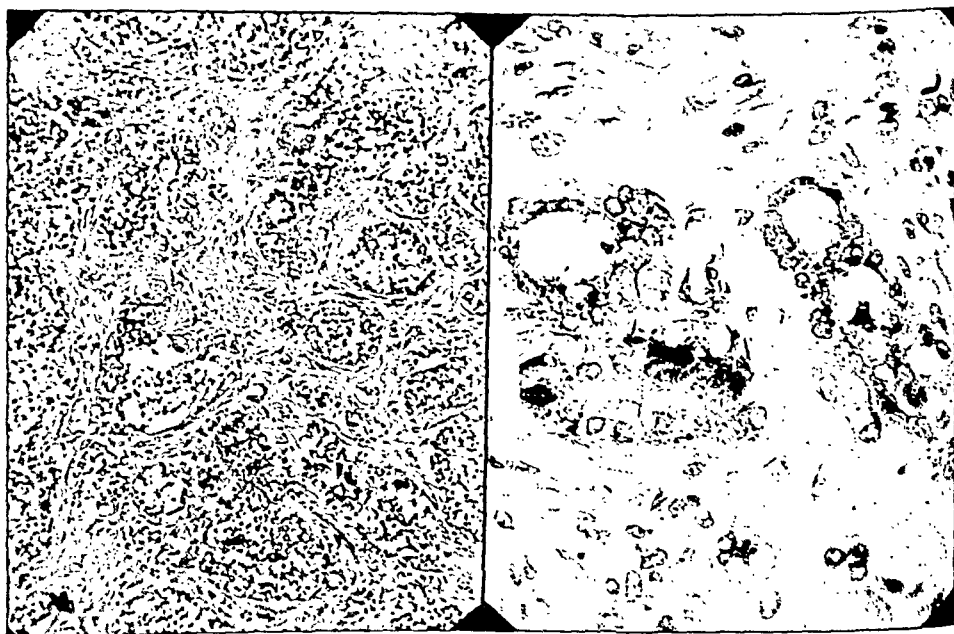


FIG. 3.—Photomicrograph ($\times 87$) showing alveolar arrangement of epithelial cells in the centre of the tumour.

FIG. 4.—Photomicrograph ($\times 325$) showing alveoli in which melanin has been produced.

nests of solid masses of epithelial cells, predominantly of basal-cell morphology, embedded in a dense fibrous stroma. The surface of the tumour at one point is covered by stratified epithelium which merges into tall columnar epithelium, composed in a single layer. This surface epithelium appears to dip into the interior where it becomes pleomorphic, merging into typical basal-cell strands and forming alveoli with clear central spaces surrounded by single-layered cubical cells with abundant cytoplasm, containing granules of brown or black pigment, which is melanin. The melanin-containing epithelium, which is mainly alveolar, appears to merge into the solid basal-cell type. In addition, there are foci where the cells are stellate and resemble ameloblasts.

"I think that the tumour is a solid epithelial odontome (adamantinoma or ameloblastoma) arising from the germinal layer of the gingivo-dental tract and producing a varied morphology in its epithelial elements, including melanoblasts, by divergent differentiation. The latter phenomenon (melanin formation) is most unusual, if not unique, in such tumours." (Figs. 3, 4.)

pigmentation in only 2 out of 500 12-year-old children, whereas in Maldon it is very common. The great majority of observers have been able to find mottling and pigmentation in the permanent dentition only, but Marshall Day (1940) has recorded a high incidence of mottling in deciduous teeth in one district in India.

It is, I think, established beyond any doubt that there is no relationship whatever between mottling and freedom from or susceptibility to caries. If one examines in South Shields a sufficiently large number of children showing enamel mottling and compares them with an equal number of South Shields children showing no sign of mottling, the incidence of caries will be found to be precisely the same in the two groups. Similarly, a given number of, say, six-year molars in South Shields showing mottling will be found to show no more and no less caries than the same number of unmottled six-year molars in South Shields—assuming, of course, continuous residence in the area by all the children concerned. This is, I think, a little surprising. It might have been expected that when a substance like fluorine produces two effects on the teeth, namely, mottling and reduction in caries liability, there would be some connexion between the two effects, but apparently there is none whatever.

Those who have subjected mottled teeth to histological examination seem to be agreed that mottled enamel is defective in its structure. Lady Mellanby (1934), for example, said "The prisms are imperfectly calcified, . . . the interprismatic substance is also deficient", whilst McKay (1929) went so far as to say that mottled enamel is "the most poorly constructed enamel of which there is any record in the literature". On the other hand, King (1944), on the basis of clinical examination of Maldon teeth, has recorded his view that, even when mottled, they are often of good structure and his figures make it clear that, in his opinion, the first permanent molars which he saw at Maldon tended to be of better structure than those which he saw in the rural parts of the Island of Lewis.

Fluorine is by no means a rare element, though I was greatly surprised to see it stated in a recent American technical journal that it is about as abundant as nitrogen or carbon. It is coming to be used very widely in industrial processes, and one of the methods employed in separating the isotopes of uranium for the atomic bomb involved the use of a fluorine compound. In this country there seem to be few communities of any size which are dependent on a water supply containing significant amounts of fluorine. Most of the larger cities get their water from moorland gathering grounds, and those waters have little chance of picking up fluorine. Those fluorine-free waters are usually soft, whereas the deep well waters in which fluorine is more likely to be found are often hard. One has, therefore, to meet the argument that the caries-inhibitory effect of waters containing fluorine may be due to hardness and not to fluorine, but I should be sorry to think that there is still any widespread belief that caries incidence is related to hardness or softness of water. In any case, there is convincing evidence from America to show that waters with caries-inhibitory properties vary so widely as regards their hardness and contain salts of all kinds as to rule out the possibility of any ingredient other than fluorine being the caries-inhibiting factor. In a symposium published by the American Association for the Advancement of Science (1946) there is a particularly convincing set of Tables, giving a detailed analysis of the water supplies of 21 towns in the U.S.A., with records of the incidence of caries and of dental fluorosis in those towns.

The fluorine content of articles of diet other than water is, generally speaking, low. An exception is tea leaves, which may contain substantial quantities; the highest of which I have seen a record was almost 1,800 parts per million. Even so, however, the amount of fluorine which one could obtain from tea would be very small. The fluorine content of fish is relatively high; a common value seems to be about 7 parts per million, but presumably a great part of that would be concentrated in the bones which would not, except in the case of the smaller fish, be eaten. The inhabitants of Tristan da Cunha, who seem fated to be quoted in every discussion about dental caries, have practically no fluorine in their drinking water, but their freedom from caries has been attributed to the large part which fish plays in their diet, and which is presumed to supply them with an appreciable amount of fluorine.

Having regard to the fact that marine products tend to have a considerable fluorine content it is rather strange that, so far as I know, no one has ascertained and recorded the fluorine content of cod-liver oil. Is its fluoride content sufficiently high to account for any beneficial effect it may have in inhibiting caries? It may be that the technical problem of estimating fluorine in an oil is a difficult one, but it would be of interest to know what the content in cod-liver oil really is.

The only other constituent of our diet which seems liable to contain any great proportion of fluorine is baking powder. In Nature, fluorides are usually found in association with phosphates, and certain baking powders contain a great deal of phosphate. I understand that those powders have tended to contain so much fluorine that the Society of Public

[February 23, 1948]

The Inhibition of Dental Caries by Fluorine

By ROBERT WEAVER, M.D., F.D.S.

AINSWORTH (1933) described the appearance of teeth observed by him in the Maldon district of Essex, where the water contains about five parts per million of fluorine. For many years previously there had been much speculation, particularly in America, as to the cause of mottled enamel. Many people suspected that the mottling was produced by some substance in the drinking water, though it is of interest to note that one writer in 1926 suggested that it might be caused by a deficiency of fluorine in water. However, about two years prior to the publication of Ainsworth's paper, it was conclusively proved that endemic mottled enamel was caused by the presence of a substantial amount of fluorine in drinking water, and Ainsworth showed that this state of affairs existed in the Maldon area. He observed that the incidence of dental caries was distinctly low in the children whom he examined, but his reference to that point takes up only about four lines in an article of seventeen pages. This is not surprising. It was not then realized that very much lower concentrations of fluorine could inhibit caries, and the readers of Ainsworth's paper, looking at the really admirable accompanying pictures of Maldon teeth, might well have said to themselves: "If this is the price which has to be paid for a lowered caries incidence, then the price is much too high." I understand that this is the view taken by quite a number of residents in the Maldon district, and that it is not unusual for young people in that area to demand that perfectly sound anterior teeth be extracted because they are so unsightly.

During the five years or so preceding the outbreak of World War II, there was an accumulation of evidence indicating that inhibition of caries could be produced by concentrations of fluorine which were too low to cause the unsightly appearance observed in teeth at Maldon and elsewhere. The person who, more than anyone else, deserves the credit for this work is Trendley Dean of the United States Public Health Service. In 1938 he showed the inverse relationship which exists between endemic dental fluorosis and dental caries prevalence, and during the next few years he, in collaboration with various colleagues, published a long series of papers which left no room for any reasonable doubt as to the caries-inhibitory effect of fluorine. When in 1944 I referred to the low incidence of caries in certain north-east Durham areas as being due to a factor F, which was probably fluorine, I did not seriously doubt Dean's conclusions; I was merely being ultra-cautious. The evidence which has accumulated since then has, however, convinced me that there is no need any longer to suspend judgment on this point.

It may be well to mention that, when we talk of fluorine in water, we are really thinking of fluoride. The other elements which combine with fluorine to form fluorides have different atomic weights, and so the amount of fluorine in 1 gramme of, say, fluor spar (calcium fluoride) is by no means the same as the amount in 1 gramme of sodium fluoride. Where quantitative measurements are concerned, we accordingly have to speak in terms of percentages or parts per million of fluorine, and not of fluoride.

It is interesting to speculate as to whether a concentration of, say, 1 p.p.m. of fluorine in water will always produce the same effect on the dental tissues, regardless of the other element with which it is combined to form a salt or regardless of the presence or absence of other substances in the water supply. Dean (1938) at one time held the view that other constituents of drinking water might perhaps have a synergistic action with the fluoride, but my impression is that he was merely refraining from ruling out any possibility, and that he really believed that fluorine produces its dental effects consistently and independently of any possible help or hindrance from other constituents of drinking water. He has stated, for example, that 1 p.p.m. of fluorine in water will result in dental fluorosis occurring in about 10% of the persons who drink that water whilst their teeth are developing, but with 2 p.p.m. of fluorine the corresponding figure for dental fluorosis will be about 60%. I have seen a little evidence to suggest that there may possibly be exceptions to a rule of this kind, but my own findings in South Shields fitted in very well with Dean's figures.

By the mottled enamel of dental fluorosis I mean paper-white patches which compare with normal enamel very much as the broken edge of a white china saucer compares with the glazed unbroken surface of the saucer. Sometimes these patches are very obvious, but sometimes they are seen only with difficulty and from a particular angle. They may not be easily seen in artificial light. They are produced by interference with the calcification of the enamel and, therefore, they never develop after eruption of the tooth, however great may be the intake of fluorine. During the post-eruptive life of the teeth, these white patches have a tendency to become pigmented, and the higher the fluorine content has been during the development of the teeth and, therefore, the greater the interference with calcification, so the greater will be the tendency for pigmentation to develop. In South Shields I saw

pigmentation in only 2 out of 500 12-year-old children, whereas in Maldon it is very common. The great majority of observers have been able to find mottling and pigmentation in the permanent dentition only, but Marshall Day (1940) has recorded a high incidence of mottling in deciduous teeth in one district in India.

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The only other constituent of our diet which seems liable to contain any great proportion of fluorine is baking powder. In Nature, fluorides are usually found in association with phosphates, and certain baking powders contain a great deal of phosphate. I understand that those powders have tended to contain so much fluorine that the Society of Public

Analysts felt that it would be desirable to have a statutory limit placed on the fluorine content of baking powder. I am under the impression that the figure they had in mind was 300 parts per million, but presumably the Minister of Health did not think that baking powder constituted a danger to health by reason of being a source of fluorine. At any rate, I have not heard of any statutory upper limit having been fixed.

Judging by the bewildering variations in the recorded fluorine content of bones and teeth, the accurate estimation of fluorine calls for a good deal of experience and skill. I once tabulated all the analyses of bones and teeth which I had been able to find in the literature, and it was clear that a great many of them must have been wrong. Thewlis (1940) gave the fluorine content of human enamel as 0.02%, and this figure corresponds so closely with the figure of 0.025% given by Bowes and Murray a few years earlier that it seems reasonable to regard it as reliable. Incidentally, it is of interest to note that Thewlis gave the fluorine content of dogs' enamel as nil, and yet the teeth of dogs hardly ever develop caries.

There was one analysis carried out in America by Armstrong and Brekhuis (1937), whose figures have been quoted over and over again as proving that the enamel of a carious tooth contains not much more than half the amount of fluorine contained in the enamel of a sound tooth. In view of the fact that their figure for the enamel of a sound tooth was only about half of that recorded by Thewlis and by Bowes and Murray, it seems unwise to quote, as many people have done, the Armstrong-Brekhuis figures as if they had settled once and for all the difference between caries-free and caries-attacked enamel. I feel that a repetition of the Armstrong-Brekhuis analysis is long overdue.

I do not intend to describe in detail my North and South Shields investigation (Weaver, 1944), but just a few of the principal findings. In North Shields water the fluorine concentration was found to be less than 0.25 p.p.m., whilst in South Shields the corresponding figure was 1.4 p.p.m. Five-year-old children in South Shields had in their deciduous teeth only 60% of the amount of caries found in similar children in North Shields—the comparison being made by recording and aggregating all decayed, missing and filled (DMF) deciduous teeth. 12-year-old children in South Shields had, similarly, 56% of the number of DMF permanent teeth found in children in North Shields. It is universally agreed that in fluorine areas the incidence of caries of the upper permanent incisors is particularly low. South Shields proved to be no exception to this rule; it showed DMF upper central permanent incisors to be only 13% of the North Shields figure, whereas for upper first permanent molars the South Shields figure was 64% of that for North Shields.

The low incidence of caries of the upper permanent incisors in fluorine areas has caused some people to put forward a suggestion which seems quite fantastic, viz. that water when taken into the mouth comes first in contact with the anterior teeth, and these teeth adsorb fluorine from the water, leaving it with insufficient to produce the same effect on the posterior teeth. If this were so, presumably upper deciduous incisors in a fluorine area would show a freedom from caries similar to that displayed by the permanent incisors, but they certainly do not. In South Shields the number of DMF deciduous upper central incisors was almost as great as the number of DMF deciduous upper first molars, whereas for the permanent dentition there were found over 50 times as many DMF upper first molars as DMF upper central incisors. The explanation which seems to me best to fit the facts is that a tooth which has little natural tendency to develop caries, such as a permanent incisor, obtains from fluorine that little extra protection which it needs. If, however, it is of a type which is prone to caries, as is an upper deciduous incisor or a molar, fluorine is not a sufficiently powerful inhibitor of caries to protect it in more than a minority of cases.

I think the most important lesson to be learned from the North and South Shields investigation is that the caries-inhibitory property of fluorine seems to be of rather short duration. The incidence of caries in an experimental and a control group is usually shown by recording the number of DMF teeth in each group, and then expressing the number in one group as a percentage of the number in the other group. Using that method, the average number of DMF permanent teeth in 12-year-old children in South Shields was 56% of the average number in North Shields. There is, therefore, some justification for saying that fluorine inhibited caries in South Shields children to such an extent as to reduce the incidence of caries by nearly half—a really remarkable result. I suggest, however, that such a comparison can be most misleading. The 12-year-old children in South Shields averaged 2.4 DMF permanent teeth, whilst the corresponding children in North Shields averaged 4.3 DMF permanent teeth. The question which really needs to be answered is "How many years does it take for the figure of 2.4 in South Shields to reach 4.3?" The answer is approximately three years. It is, of course, true that during those three years the figure of 4.3 in North Shields is also increasing, but the fact remains that at 15 years of age children in South Shields have the same average amount of caries as is found in North Shields at 12 years of age. A further investigation into the dental condition of adults in the two towns showed that in them caries was postponed for about five years. I should like it to be clearly under-

stood, however, that when I refer to fluorine as having the power only to postpone the onset of caries for three to five years, I do not mean that this holds good for each separate tooth or for each separate individual. It is a statement, from the epidemiological angle, of what increase in caries incidence may be expected in a certain group in a certain number of years, but it gives no information whatever as to the increase in caries incidence which may be expected in any individual member of the group. I suggest, however, that when any given regime or procedure is claimed to be of value in reducing the incidence of caries, those whose concern is with the manifestations and effects of dental disease in the community should not be satisfied with the traditional kind of evidence; evidence regarding the duration of the protection rather than that based on percentage comparisons should be asked for.

I might add, in passing, that if the protection given by fluorine in South Shields had not been shown to be of quite brief duration, members of the dental profession would have been faced with an embarrassing question. That question would have been "If the incidence of dental caries in South Shields is so very much less than in North Shields and if dental disease is inimical to health, why is it that there seems to be no evidence that the South Shields population is healthier than the population of North Shields?" The answer, of course, is that the figure of 56% which I have given in connexion with the findings for 12-year-old children is misleading; that there is in fact no very striking difference in the incidence of caries in the two towns, and therefore that there is no reason to expect South Shields to have a better health record than North Shields.

Having indicated that only a limited beneficial effect can be expected from the ingestion of fluorine in drinking water, something needs to be said about the possibility of its doing any harm. A good deal has been written, notably by Roholm (1937), about the toxicology of fluorine, but he was concerned mainly with effects produced by the quite exceptional conditions experienced by workers in cryolite—a fluorine compound obtained in Greenland and refined in Denmark. There have been reports from India of severe skeletal disabilities, apparently resulting from the ingestion of fluorine, but the water supplies invariably contained unusually high concentrations of fluorine—far beyond anything which is found in this country. There has been a small-scale investigation in England by Kemp, Murray and Wilson (1942), in the course of which radiographs were taken of a number of spines with a view to discovering whether spondylitis deformans might be related to fluorine intake. The investigators concluded that spondylitis deformans was fairly common, whether or not there was evidence of dental fluorosis. They added that fluorine in soil and water, in association with defective nutrition, may favour such maldevelopment; they did not, however, seem satisfied that it often does so.

McClure (1944) found no relationship between fluoride exposure and fracture incidence. He considered that his findings pointed to the unlikelihood of skeletal development being adversely affected by continued ingestion of drinking water containing up to 6 p.p.m. of fluorine.

It is claimed by Dagmar Wilson (1941) that fluorine areas show an unusually high incidence of goitre, but I did not find goitre to be prevalent in north-east Durham. If the intake of fluorine is very high, it is possible that damage to the kidneys may result, and there have been statements to the effect that fluorine considerably lengthens the clotting time of the blood, though this has been disputed. Fluorine is a very toxic substance, and if ingested in large quantities it will do considerable harm, but the evidence which I have seen has given me no reason to think that, apart from the rather unsightly appearance of the teeth in some areas, there would be any harmful effect produced by the long-continued ingestion of any fluorine-containing water found in this country.

Does fluorine produce its caries-inhibitory effect during the pre-eruptive or the post-eruptive life of the teeth? If it were produced during pre-eruptive life, presumably it could only be by way of effecting some modification in the structure of the teeth, making them more resistant to attack. One thinks, for example, of the way in which the addition of very small amounts of other substances affects the properties of steel, producing stainless steel with its high power of resistance to corrosion, which is a chemical attack, and one wonders whether the incorporation in the developing enamel of quite small amounts of fluorine so alters its chemical constitution as to render the enamel more resistant to chemical attack. Laboratory experiments have been carried out in which powdered enamel has been treated with various fluorides, and an apparent reduction in enamel solubility has thereby been secured. It is, however, doubtful whether conclusions from these *in vitro* experiments are valid for teeth in the mouth; it seemed, for example, as if lead fluoride was particularly effective in the laboratory in reducing enamel solubility, and yet topical application of lead fluoride solution to teeth in the mouth appeared, according to one investigation, to produce no beneficial effect.

An effect produced by fluorine during the post-eruptive life of the teeth might result either from an increase in their resisting power or from a change in their environment—in

other words, it could either strengthen the defence or weaken the attack. I, therefore, examined 800 children who had been born outside the north-east Durham area and had come to live in it at various ages. It was only the six-year molars which were curious in numbers sufficient to provide any evidence of value, and, so far as caries of those teeth was concerned, it seemed to be established that, up to and including the age of about 5 years, it did not matter whether the child's residence in the fluorine area had been long or short. To put it in another way, children who came to live in the fluorine area appeared to have an average caries incidence in their six-year molars which was quite independent of the age at which they arrived there, provided—and this is important—provided they got there before the age of 6. Now this seemed to indicate that, in order to obtain protection for the six-year molars, it was not essential that the child should have been ingesting fluorine for a considerable time; what did seem to be essential for maximum protection was that the child should have ingested fluorine for a period, though probably only for quite a brief period, before the eruption of the six-year molars. However, children arriving in the fluorine area at 6 years of age appeared to derive some benefit, whilst those arriving at 7 years of age or later apparently derived no benefit at all so far as protection of their six-year molars was concerned. It seemed, therefore, that if fluorine confers on the tooth any protection during its post-eruptive life, it is only during a quite brief period following eruption that such protection can be acquired. This is not easy to accept, though in correspondence which I have had with Bibby, he has put forward an ingenious theory to account for it. Briefly, it is this. Newly erupted enamel is prepared to adsorb a number of different substances from its environment. If that environment contains fluorine, the enamel will adsorb fluorine; if the environment does not contain fluorine the enamel will adsorb another substance or substances which will, so to speak, exhaust its adsorptive capacity and so render it incapable of taking up fluorine even if it gets the chance to do so later on.

Therefore, the examination of those 800 children did not provide a perfectly definite answer to the question of pre-eruptive *versus* post-eruptive influence. It appeared to me probable, on the basis of my findings, that the protection was acquired during a late stage in the pre-eruptive life of the tooth, but I could not rule out the possibility that it might be acquired just after eruption. At first I thought that the uncertainty was due to the fact that 800 children did not constitute a sufficiently large number when divided into age-groups, but I am now satisfied that the same uncertainty would have followed an examination of ten times that number of children, if it had been possible to find such a number fulfilling the necessary conditions. The uncertainty is really due to the fact that, although it was possible for me to get precise information about the time of a child's arrival in the fluorine area, I could not say, in the case of a child who had arrived there somewhere about the age of 6 years, which, if any, of its six-year molars had erupted before its arrival. There seems no way of overcoming this difficulty in any investigation of the type which I carried out but it can, and I expect will, be overcome by utilizing the data from those American communities where fluorine is now being added to the water supplies. If, immediately before the commencement of the addition of fluorine, children have been dentally examined and a record has been made of which teeth have erupted and which have not, then it will be possible to compare in due course the caries incidence of those teeth which were erupted before the addition of fluorine with the incidence in those which were unerupted.

There have been in America several investigations based on the same idea as the one I carried out. Some of them have been done in areas where there was a change in the fluorine concentration in the water supply—sometimes from high to low fluorine content, and sometimes from low to high fluorine. Others have been concerned with persons whose place of residence had changed. None of them, however, has seemed to me to provide convincing results; indeed, the conclusions of different observers have given rise in my mind only to confusion.

A certain amount of work has been done with a view to finding out whether fluorine produces any significant change in the environment of the teeth. There seems to be general agreement that the activity of salivary amylase is not affected by fluorine even in quite high concentrations. Children drinking water containing 1.8 p.p.m. of fluorine were recorded by McClure (1939) as having just the same salivary amylolytic activity as children drinking fluorine-free water. *Lactobacillus acidophilus* counts have not always given consistent results but, on the whole, children drinking water containing significant quantities of fluorine tend to show considerably lower *Lactobacillus* counts than do those using fluorine-free water. Whilst, however, many people accept it as established that there is an association between high *Lactobacillus* counts and high caries activity, it is by no means accepted that this relationship is one of cause and effect—or rather, one might say it is not certain which is cause and which is effect.

With a view to reducing the caries incidence in areas where there is little or no fluorine in the drinking water, four methods of utilizing the caries-inhibitory property of fluorine

have been suggested. They are: (1) Addition of fluoride to drinking water; (2) administration of fluoride in solid form; (3) topical application of fluoride solution to the teeth; (4) incorporation of fluoride in dentifrices.

Let us consider first the addition of fluoride to drinking water. At the present time there are eight communities in the U.S.A. and Canada where fluorine is being added to the domestic water supply for the purpose of studying the effect on dental caries. The first of these community experiments was begun at Grand Rapids, Michigan, in January 1945, and a preliminary analysis of the dental findings so far has been made but, as yet, nothing has to my knowledge been published. The fluorination of water does not appear to present any technical difficulty, and the cost is not high. One American estimate of the expenditure is that it would amount to about 7½ cents per head of the population per annum.

In spite of the ease and cheapness of this method it is not, however, one to be adopted without very serious consideration. There are many people who would object strongly to what they would regard as tampering with their water supply, and public opinion in a matter of this kind cannot safely be ignored. I have heard of one American community where there had been some publicity about a proposal to fluorinate the local water supply, and some time later the Public Health Department began to receive complaints from residents that since the addition of fluorine to the water their teeth had gone to the dogs. In fact, the project had never got beyond the stage of talking about it, and no fluorine had ever been added.

It has not, so far as I know, ever been suggested that a community water supply should have its fluorine content raised to a level above 1 p.p.m. That being so, I think there is no reason to anticipate that the addition would do any harm, but mention should be made of other objections to the procedure.

The first is that it is regarded, not unnaturally, by many water engineers as a clumsy method. To add fluoride to the whole of a town's water supply in order to fluorinate the comparatively small proportion of that supply which is actually drunk seems to them uneconomical. If it is argued that the whole of a town's water supply has to be chlorinated in order that the inhabitants may drink chlorinated water and thereby obtain protection against water-borne diseases like typhoid fever, a further objection would be that the protection afforded by chlorination is enjoyed by the whole community. On the other hand, it may well be that fluorination would not benefit in the least the residents whose teeth would have been already formed at the time fluorination was commenced, and even in the case of children whose teeth would be exposed to fluorine during the whole period of their development, there would be quite a number who would apparently derive no benefit. To illustrate this point, I might mention that the first four children whom I examined in South Shields had between them 41 DMF teeth. It could be argued that, if they had not been ingesting fluorine the number of their DMF teeth would have been much more than 41, but it must be admitted that if those four children had derived any benefit from fluorine, the benefit was by no means obvious.

Next, it might be claimed that "doctoring" of the water supply would be justified if it could be established that some permanent or long-continued reduction of caries could be achieved, but that it is not justified if the reduction of caries is merely a transient effect—a delaying action rather than a prevention of caries.

Finally, it would be argued that the amount of fluorine ingested from water depends not only on the concentration of fluoride in the water, but also on the quantity of water which is drunk. In this respect there are substantial differences between different individuals and also, in the same individual, there may be differences depending on the season of the year. In order to ensure a uniform intake of fluorine from water for the whole year it might be necessary to vary the content between say 0·7 p.p.m. at the height of summer and perhaps twice that concentration in the depth of winter. A complication is thus introduced, and objections would doubtless be made to the content ever being raised above 1 p.p.m.

We turn now to the second method, namely, the administration of fluoride in solid form. There are precedents for a procedure of this type, notably the iodizing of salt for the prevention of goitre, and the addition of calcium to flour. Some enthusiastic advocates of water fluorination claim that the beneficial effect of drinking water which contains fluorine is the result of the fluorine being adsorbed by the teeth during its passage through the mouth, rather than from any effect produced by the fluorine after it is swallowed. They would accordingly argue that fluoride passing through the mouth in solid form could not readily be adsorbed by the teeth and would, therefore, be comparatively ineffective. It seems to me, however, that the evidence for their argument is very thin and, I think, therefore, that the ingestion of fluoride in solid form by those who want it is much to be preferred to the compulsory ingestion of fluorine in water both by those who would welcome, and those who would strongly object to, such a procedure. Incidentally, those who wish to take fluorine could take it either in solid form or as an addition to the household water, but it is probable

other words, it could either strengthen the defence or weaken the attack. I, therefore, examined 800 children who had been born outside the north-east Durham area and had come to live in it at various ages. It was only the six-year molars which were carious in numbers sufficient to provide any evidence of value, and, so far as caries of those teeth was concerned, it seemed to be established that, up to and including the age of about 5 years, it did not matter whether the child's residence in the fluorine area had been long or short. To put it in another way, children who came to live in the fluorine area appeared to have an average caries incidence in their six-year molars which was quite independent of the age at which they arrived there, provided—and this is important—provided they got there before the age of 6. Now this seemed to indicate that, in order to obtain protection for the six-year molars, it was not essential that the child should have been ingesting fluorine for a considerable time; what did seem to be essential for maximum protection was that the child should have ingested fluorine for a period, though probably only for quite a brief period, before the eruption of the six-year molars. However, children arriving in the fluorine area at 6 years of age appeared to derive some benefit, whilst those arriving at 7 years of age or later apparently derived no benefit at all so far as protection of their six-year molars was concerned. It seemed, therefore, that if fluorine confers on the tooth any protection during its post-eruptive life, it is only during a quite brief period following eruption that such protection can be acquired. This is not easy to accept, though in correspondence which I have had with Bibby, he has put forward an ingenious theory to account for it. Briefly, it is this. Newly erupted enamel is prepared to adsorb a number of different substances from its environment. If that environment contains fluorine, the enamel will adsorb fluorine; if the environment does not contain fluorine the enamel will adsorb another substance or substances which will, so to speak, exhaust its adsorptive capacity and so render it incapable of taking up fluorine even if it gets the chance to do so later on.

Therefore, the examination of those 800 children did not provide a perfectly definite answer to the question of pre-eruptive *versus* post-eruptive influence. It appeared to me probable, on the basis of my findings, that the protection was acquired during a late stage in the pre-eruptive life of the tooth, but I could not rule out the possibility that it might be acquired just after eruption. At first I thought that the uncertainty was due to the fact that 800 children did not constitute a sufficiently large number when divided into age-groups, but I am now satisfied that the same uncertainty would have followed an examination of ten times that number of children, if it had been possible to find such a number fulfilling the necessary conditions. The uncertainty is really due to the fact that, although it was possible for me to get precise information about the time of a child's arrival in the fluorine area, I could not say, in the case of a child who had arrived there somewhere about the age of 6 years, which, if any, of its six-year molars had erupted before its arrival. There seems no way of overcoming this difficulty in any investigation of the type which I carried out but it can, and I expect will, be overcome by utilizing the data from those American communities where fluorine is now being added to the water supplies. If, immediately before the commencement of the addition of fluorine, children have been dentally examined and a record has been made of which teeth have erupted and which have not, then it will be possible to compare in due course the caries incidence of those teeth which were erupted before the addition of fluorine with the incidence in those which were unerupted.

There have been in America several investigations based on the same idea as the one I carried out. Some of them have been done in areas where there was a change in the fluorine concentration in the water supply—sometimes from high to low fluorine content, and sometimes from low to high fluorine. Others have been concerned with persons whose place of residence had changed. None of them, however, has seemed to me to provide convincing results; indeed, the conclusions of different observers have given rise in my mind only to confusion.

A certain amount of work has been done with a view to finding out whether fluorine produces any significant change in the environment of the teeth. There seems to be general agreement that the activity of salivary amylase is not affected by fluorine even in quite high concentrations. Children drinking water containing 1.8 p.p.m. of fluorine were recorded by McClure (1939) as having just the same salivary amylolytic activity as children drinking fluorine-free water. *Lactobacillus acidophilus* counts have not always given consistent results but, on the whole, children drinking water containing significant quantities of fluorine tend to show considerably lower *Lactobacillus* counts than do those using fluorine-free water. Whilst, however, many people accept it as established that there is an association between high *Lactobacillus* counts and high caries activity, it is by no means accepted that this relationship is one of cause and effect—or rather, one might say it is not certain which is cause and which is effect.

With a view to reducing the caries incidence in areas where there is little or no fluorine in the drinking water, four methods of utilizing the caries-inhibitory property of fluorine

Section of Neurology

President—C. WORSTER-DROUGHT, M.D.

[February 5, 1948]

Electromyography

By P. BAUWENS

Director of the Department of Physical Medicine, St. Thomas's Hospital, London

A MORE scientific approach to the study of electric changes in contracting muscle became possible with the advent of Lippmann's capillary electrometer (invented 1875) and later Einthoven's string galvanometer (invented 1906). The moving parts of these instruments were sufficiently light to follow the rapid variations of potential. They moreover allowed records to be made so that analysis of both wave-form and frequency became possible.

Limited though these instruments were, they served their masters well, and enabled Piper and more recently Adrian, Bronk and Matthews to lay the foundation on which clinical electromyography must forever rest.

Recent investigators in the field of electrical activity in muscles and nerves have enjoyed the great advantage derived from the development of valve amplifiers. Well-designed equipment of this type can magnify fluctuating potentials applied to it as much as a million times without appreciable distortion of wave-form. Once the potentials have attained a sufficient magnitude they can be measured with appropriate instruments; translated into sound in a loud speaker; projected as visible waves on to the screen of a cathode-ray oscilloscope and permanently recorded on gramophone discs or photographic films, or again—within certain limits of frequency—on paper by means of electromagnetic pen recorders.

The equipment recently constructed by Peter Styles at St. Thomas's Hospital has two completely separate channels each with its own amplifying, measuring, monitoring, calibrating and recording devices (fig. 1). It also incorporates an electrical stimulator which is synchronized with the sweep of both monitoring cathode-ray oscilloscopes.

From its history it is obvious that electromyography as it is known to-day is a direct application of electrophysiology to clinical medicine.

The intimate mechanism of production of biological electricity has for many decades attracted the attention of biophysicists and many are the hypotheses which

that the latter method, involving the making-up of a solution of given strength, would be much the less popular. The fluorine to be taken in the solid form might well be incorporated in tablets of prescribed composition, containing say 1 mg. of fluorine as fluoride, for use in an area with a fluorine-free water. If the water contained some fluorine, the tablets should contain proportionately less. It has been suggested that bone meal would serve as a source of fluorine to be taken in solid form, but analyses of bone meal show considerable variations in fluorine content, and so this method of giving fluorine is rather lacking in precision.

The topical application of fluorine, that is, the painting of the teeth with a fluoride solution, has been carried out on a considerable scale in America. In this country an investigation has been carried out at a residential school in Cheshire by Professor Stones of Liverpool, assisted by members of his staff at the Dental Hospital. The experiment itself was completed some considerable time ago, but there has been a delay in obtaining a statistical analysis of the results. Although many of the reports from America are most enthusiastic about this procedure, I should prefer to suspend judgment as to its value until Professor Stones' figures are available. One American investigation by Arnold, Dean and Singleton (1944), carried out in the U.S. Coast Guard Academy, led the investigators to conclude that 'there is no evidence in this study that a single topical application of a fluoride solution to the teeth of young adults as here carried out would result in reduction of dental caries incidence'.

On the other hand, there are numerous American reports of striking effects having been produced in children by multiple applications of a 2% sodium fluoride solution. A typical report is that by Galagan and Knutson (1947) a few months ago, in which they record having applied sodium fluoride solution to the teeth on one side of the mouth of 1,555 children—the teeth on the untreated side acting as controls. They state that the incidence of initial caries in permanent teeth which were non-carious at the time of treatment with 2, 4 and 6 applications was, after an interval of a year, 21·7, 40·7 and 41% less respectively in treated than in untreated teeth. They believe that four topical applications of sodium fluoride, preceded by dental prophylaxis, afford maximum reduction in dental caries incidence.

One of the reasons for hesitation in accepting unreservedly the claims for the value of topically applied sodium fluoride is the fact that the results of its application to mandibular teeth have been usually much less beneficial than in the case of teeth in the upper jaw. Various attempts have been made to explain why this should have happened, but the explanations do not seem to be entirely convincing.

As for the addition of fluoride to dentifrices, it was suggested in an editorial article in the *British Medical Journal* that the time might come when legislation should provide for the compulsory inclusion of specified amounts of fluorine in every dentifrice sold to the public. I know of only one experiment designed to test the value of fluorine used in this way; it was carried out by Bibby (1945). Both a liquid and a paste dentifrice were supplied, sodium fluoride being incorporated either in 0·01% or 0·1% strength. The users were dental students and orphanage children. Bibby reported that no evidence of a reduction of caries activity was found—a result which did not surprise him so far as the young adults were concerned, but which was quite contrary to his expectations regarding the children. I have heard recently of one British firm contemplating the manufacture of a fluoride-containing toothpaste, but up to the present I have seen no evidence which would justify encouragement of such a venture.

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responses of these muscle fibres are simultaneous, the electrical disturbance caused by the excitation of a motor unit is substantially a large amplitude diphasic wave which after amplification evokes a popping noise from a loud speaker.

Even the weakest possible voluntary movement of a muscle appears to entail the excitation of several motor units but the activity of these under normal conditions is not synchronized. On the contrary, Nature seems to have been at pains to ensure that they not only fire out of step but also that adjacent ones have different firing frequencies. All the same, there is some evidence that during maximal exertion a certain rhythm somewhat resembling a beat frequency develops. Piper, who first described this phenomenon in man, insisted that the basic frequency approached 50 per second.

When the clinic replaces the laboratory, and the patient the experimental animal, the method of leading off these potentials has to be modified, and surface electrodes or needle electrodes are employed. The former record, at the level of the skin, the integrated potentials caused by the electrical disturbances in a large and ill-defined muscle mass in the field between the two electrodes which may be several inches apart. This method is useful for cursory examinations and where collective effects are investigated. Its lack of accuracy and the fact that some electrical fluctuations of short duration cannot be picked up by this method, make the second method the one of choice. Here the two electrodes are concentrically disposed. Such an arrangement is conveniently obtained by fitting an insulated metal shaft into the lumen of an ordinary syringe needle. It is important to realize that with this method one obtains samples of electrical disturbances in a very restricted volume of the tissues but that these can be localized with great precision.

When making electromyographic observations it is important to bear in mind the structures involved. These are diagrammatically illustrated in fig. 2. Two motor units are represented, MU¹ and MU², with the nerve fibres supplying them: NF¹ and NF² respectively.

Under resting conditions in a normal subject, no electrical activity is detected either by means of the surface electrodes (SE) applied to the skin or the needle electrodes (NE) inserted into motor unit (MU¹).

Were motor unit 1 to enter into activity as the result of volition, then all the muscle fibres in this unit would contract simultaneously. Each would supply its own contribution of electrical potential and as a result a popping sound would issue from the loud speaker (LS) while a discrete diphasic wave (fig. 3) would be produced on the screen of the cathode-ray oscilloscope (CRO) and on the paper of the pen recorder (PR). Increased exertion would first cause an increase in the repetition frequency of this diphasic discharge and then bring other motor units into play. It is interesting to note that supposing motor unit 2 (MU²) became active, the discharges from this would not be synchronized with those of motor unit 1 (MU¹) and would probably have a different frequency.

The asynchronous activity of motor units when integrated expresses itself as an interference pattern on the screen of the CRO and on a penned record (fig. 4) and an irregular rumble in the loud speaker.

Synchronized activity in motor units occurs as the result of tendon reflexes (fig. 5), electrical stimulation of nerve trunks and, as will be seen later, under some pathological conditions.

On maximal exertion both the wave graph and the sound are sustained. Failure to obtain this is highly suspicious of inactivity on the part of a large proportion of motor units.

have emerged from their labours. If the theoretical considerations concerning the nature of action potentials are purely academic, a knowledge of their possible origin and the factors which may evoke them has none the less a practical value.

It has long been recognized that most vital processes, if not electrical by nature, are often inseparably associated with electrical phenomena. In common with other living systems, excitable tissues are electrically polarized. This means that on either side of a limiting surface which appears to keep them apart there exist positive and negative charges.

Nerve and muscle fibres share the distinction of being polarized in this manner—negatively at the centre and positively on the outside. That these potential differences exist can easily be shown by means of a sensitive galvanometer connected across the raw and the uninjured surfaces of a recently cut muscle.

During activity these charges appear to neutralize one another, as if the insulating properties of the structure separating them had broken down. The sudden disap-

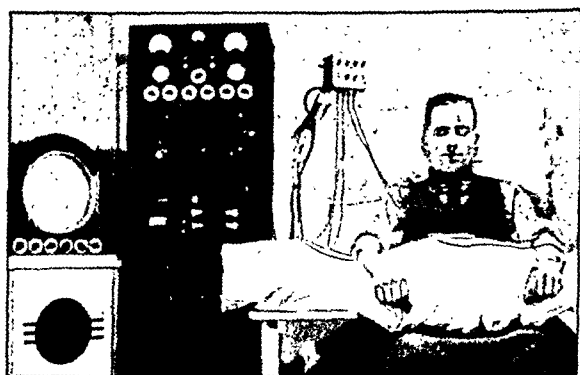


FIG. 1.—Two-channel electromyographic equipment. Centre: The amplifier. Left: The loud speaker and large cathode-ray oscilloscope. Right: Double input head with two pairs of suction surface electrodes symmetrically applied as for comparison of electrical activity in extensors. (Vacuum pump not shown.)

pearance of the localized charges invariably results in a readjustment of electrical balance in the surrounding structures which virtually constitute an external circuit. The disturbances thus produced are the very ones with which we are concerned.

In the physiological laboratory, where precision experimentation can be carried out by dissection and the use of conditioning drugs, it is possible to demonstrate that local activity in a single nerve or muscle fibre is accompanied by a rapid variation of electrical potential. Since the zone of activity is propagated along the fibre, it follows that the associated electrical by-products will similarly move along. When the electrical phenomena are recorded by means of two electrodes in contact with the fibre, the influence of the propagated electrical potential on each one in turn produces the typical diphasic wave which has come to be called spike potential.

Again, in the laboratory the simultaneous stimulation of two or more fibres is feasible. In the case of muscle the integrated electrical effects of several fibres manifest themselves—with certain reservations—by an increase in the amplitude of the resulting diphasic wave. In the intact animal, however, the smallest unit which normally enters into activity as the result of volition is not a single muscle fibre but a group embodying as many as 300 or more fibres supplied by one motor nerve fibre. As the

of great diagnostic and prognostic significance in peripheral nerve injuries. They are of assistance in differentiating quantitatively between complete and partial denervation and qualitatively between paralysis due to transient nerve block and that due to axon degeneration.

In the presence of normal motor unit activity on volition and either silence or fibrillation potentials at rest, the electromyographic interpretations are moderately simple. Unfortunately a whole gamut of other electrical disturbances of less easily recognizable origin can come to light. They may occur spontaneously or be provoked by manipulation or movement of needle electrodes.

The spontaneous ones may range from the fibrillation potentials, already discussed, to intermittent trains of oscillations of high frequency. In between these two extremes there are discrete, high amplitude discharges of either a diphasic or highly complex



FIG. 4.—Electrical activity in a normal muscle with increasing exertion.

type. Again, they may come at random, rhythmically or in surges. Many of them can be evoked by movements of a needle electrode, attesting to their peripheral origin.

At times the frequency is sufficiently high to give rise in the loud speaker to a quasi-musical sound.

A medley of these may occur in motor neurone diseases, as if progressive destruction of a neurone led to a state of irritability at the myoneural junction of which fasciculation is a clinical expression.

The repetitive character of both the fasciculation potentials and the fibrillation potentials suggests some relationship. Fasciculation might possibly be a kind of synchronized fibrillation occurring at a time when the terminal arborization of the diseased nerve fibre is still apt to transmit impulses from one myoneural junction to another.

By referring to fig. 2 and supposing the two motor units depicted to be at different stages of progressive destruction we can in a somewhat over-simplified manner envisage the electromyographic picture to which this would give rise.

At first, motor unit 1 might be diseased and, before complete denervation, might give rise to fasciculation. At that time intact motor unit 2 could still produce normal action potentials on volition. At a later date, while motor unit 2 goes through the fasciculating phase, motor unit 1 might have reached denervation and the individual muscle fibres composing it might produce typical fibrillation potentials. This would give rise to both phenomena at the same time.

The picture becomes even more complicated when the cause of the progressive neurone destruction acts as an irritative process either in part or at one stage. Referring again to fig. 2, suppose a zone of compression at X. This might cause irritation of MU¹ and the setting up of a trigger zone of the type described by Kugelberg, possibly coupled with a simple nerve block above it. This might cause spontaneous discharges in the muscular part of the unit as well as an occasional burst of action potentials on

After section of a nerve fibre the muscle fibres supplied by it naturally lose their power of contracting on volition as well as the collective electrical disturbances associated with this. It does not, however, spell the end of activity of the individual

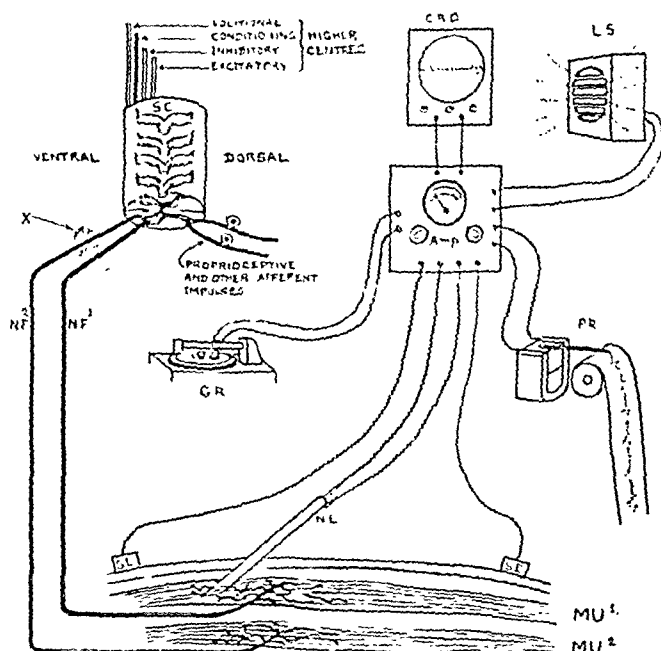


FIG. 2.—Anatomical structures and electrical equipment involved in electromyographic investigation diagrammatically represented. SC: Lateral view of section of spinal cord. MU¹ and MU²: Two motor units. NF¹ and NF²: Nerve fibres respectively supplying MU¹ and MU². SE: Surface electrodes. NE: Needle electrodes. Amp: Amplifier with output meter. LS: Loud speaker. CRO: Cathode-ray oscilloscope. GR: Gramophone disc recorder. PR: Electromagnetic pen recorder. X: Site of lesion.

muscle fibres composing the motor unit. After a lapse of approximately three weeks these fibres may begin to enjoy an autonomous life of which one manifestation is a rhythmic activity termed "fibrillation". This gives rise to repetitive potentials of short duration and small amplitude which impart a ticking quality to the loud speaker and assume the shape of small spikes on the screen of the cathode-ray oscilloscope. These characteristics make fibrillation potentials easily distinguishable from normal motor unit activity.

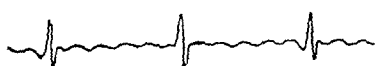


FIG. 3.—Three discrete biphasic potentials in normal muscle resulting from electrical stimulation of nerve.

FIG. 5.—Electrical activity in quadriceps muscle as a result of tendon-jerk.

The numerical reduction in normal action potentials on maximal exertion or their total absence, coupled with the presence or absence of fibrillation potentials, can be

experience we have been able to confirm this in advanced cases of progressive muscular atrophy, and anterior poliomyelitis, not only when using two needle electrodes in the same muscle but also when using four surface electrodes on the skin overlying a muscle.

Fig. 8 shows two tracings taken simultaneously from two pairs of surface electrodes disposed on the sole of the foot of a patient suffering from progressive muscular atrophy. The synchronized action of the intact motor units can be deduced not only from the timing of the diphasic waves but also from the high amplitude of the individual discharges.

Buchthal and Clemmessen also draw attention to an interesting phenomenon in this connexion. On fatigue, the motor units drop out one by one thus producing a

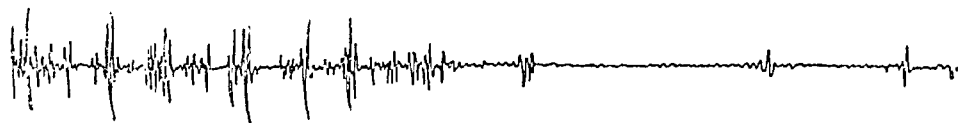


FIG. 7.—Electrical activity at rest provoked by manipulation of the neck in a case of suspected disc lesion.

decrease both in amplitude of the individual diphasic waves, but also in the frequency.

It is possible that better acquaintance with these phenomena may eventually assist in the early differential diagnosis of simple polyneuritis and motor neurone diseases.

In myopathies where the muscular weakness results from a diminution in the number of effective muscle fibres rather than from a numerical reduction in whole motor units, a decrease in the amplitude of the spikes can be expected. As Kugelberg points out, in myopathies the emphasis is on spikes with narrow bases and of small amplitude but—except in advanced cases—of frequencies approaching that encountered in normal muscles.

The few congenital amyotonias I have had the opportunity of examining have revealed the existence of sustained electrical activity simultaneously in antagonistic groups of muscles even though these appeared flaccid.

Buchthal and Clemmessen have studied the electrical activity at rest in some of the

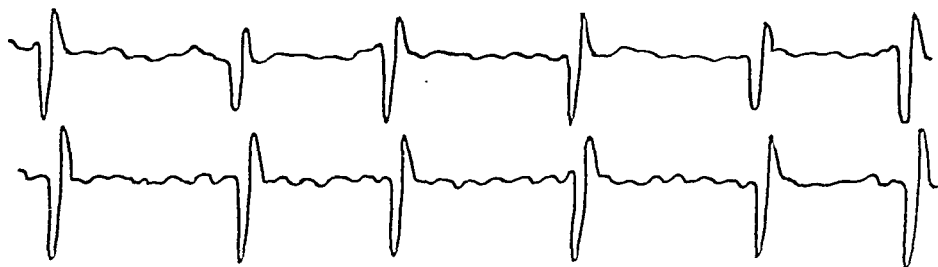


FIG. 8.—Simultaneous tracings showing synchronized activity throughout the plantar muscles demonstrated by the use of two independent pairs of electrodes applied to the sole of the foot during attempt at flexion of toes in a case of advanced progressive muscular atrophy.

painful conditions in muscles, associated with palpable alterations in the consistency of the muscles. It would appear that this activity can be abolished by injection of a

volition when the block is jumped—as may happen intermittently (Hodgkin's extrinsic potential).

An even more complex set of conditions worthy of some attention might be set up at the level of a lesion of both irritative and destructive nature. It is now generally accepted that the spike potential in one nerve fibre can stimulate an adjacent fibre provided the threshold of excitability of the receptor fibre is sufficiently lowered.

Recently Granit, Leskell and Skoglund devised ingenious experiments which enabled them to demonstrate that this cross interaction occurred not only at the cut end of nerves but also as the result of pressure or crushing. The practical significance of their results did not escape these workers. They concluded that "an injured or compressed region forms a critical point at which impulses can be reflected centrifugally or centripetally by engaging other fibres by interaction".

Referring once more to fig. 2, it means that compression or injury, say at point X, might cause impulses conducted from the cord in nerve fibre 1 to stimulate nerve fibre 2. The net result would be activity of both motor units which would not be perfectly synchronized on account of the delay at the artificial synapse. Hyperventilation with the consequent lowering of the threshold of excitability would increase the effect.

Arvanikati, while studying "ephapses" as she calls these artificial synapses, found that under certain conditions her cut nerve preparation became the seat of oscillating potentials.

In practice it is found that a prolapsed disc or a constricting lesion produces electrical activity at rest in the muscles supplied by the root or trunks affected by the pressure (fig. 6). The problem here is, should the patient be examined during the acute or chronic

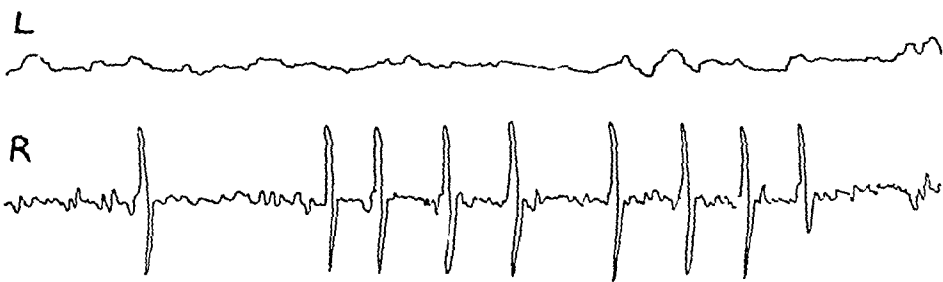


FIG. 6.—Simultaneous tracings of electrical activity in R. and L. biceps showing spontaneous activity in R. biceps presumed to be due to an intervertebral disc prolapse.

stage of the condition and how should one obtain general relaxation of the muscles while lowering the threshold of excitability at the level of the lesion? It may some day prove possible to send antidromic volleys up one nerve and demonstrate, in the presence of a lesion, an electromyographic echo in a muscle supplied by other nerve fibres.

At present it is sometimes possible to record an increase in the activity at rest when an appropriate portion of the spine is manipulated so as to increase the pressure in the case of disc lesions, or the shoulder girdle in the case of upper thoracic outlet syndromes (fig. 7).

Affections of the cord also appear to have their own characteristics. Buchthal and Clemmessen find that in muscle wasting and paresis of cord origin there is a tendency to synchronization of activity in motor units which are still intact. In our limited

Section of Dermatology

President—J. E. M. WIGLEY, F.R.C.P.

[December 18, 1947]

Rheumatic Nodules: Granuloma Annulare.—R. E. BOWERS, M.B.

Mrs. R. S., aged 25.

In 1943 a subcutaneous swelling appeared just below the left olecranon process. Shortly afterwards a similar tumour appeared at the same site on the opposite side.

The patient had been healthy until January 1939, when she was admitted to St. Giles' Hospital with acute bilateral salpingo-oophoritis, a left-sided pyosalpinx and a pelvic abscess. No gonococci found. She was treated conservatively and discharged in March 1939. In 1943 she began to develop rheumatism in the feet, and subsequently in the joints. About the same time the tumours appeared on the forearms.

When first seen at St. Thomas's Hospital in October 1945 she had two lobulated firm subcutaneous swellings in the positions described, freely mobile under the skin and just movable over the bone. Section of the tumour on the left side showed principally masses of endothelial cells and an area of necrosis surrounded by endothelial cells arranged in palisade fashion. The histological appearances suggested granuloma annulare and this was confirmed by Dr. Freudenthal.

The patient was next seen in September 1947, when she also had a small flat plaque on the right foot which clinically suggested granuloma annulare. One of the main lesions was excised.

The W.R. and gonococcal complement fixation tests are negative.

Histology.—(1) *Specimen taken in 1945:* A small area of necrosis with endothelial cells in palisade arrangement at the periphery. Elsewhere masses of endothelial cells without necrosis, and much young connective tissue. In the endothelial masses many new blood vessels. (2) *Tumour excised in September 1947:* Similar to the above except that the areas of necrosis are many and large, and the whole process is accompanied by extensive fibrosis.

Comments.—Large nodules of this type occur in chronic rheumatoid arthritis. In their early stages they show much endothelial proliferation and new vessel formation, but later there appear centres of necrosis surrounded by endothelial cells in a palisade arrangement. Fibrous tissue is laid down round these foci, which eventually may undergo cystic degeneration.

At the stage of necrosis the histological picture may be indistinguishable from that of well-developed granuloma annulare. Dr. Parkes Weber in "Rare Diseases" (1947) quotes Freudenthal as saying that this is so. Dr. A. J. Rook has recently drawn my attention to H. Keil's article (*Medicine*, 1938, 17, 261) in which this resemblance is mentioned, and Dr. Freudenthal has pointed out another reference to it, i.e. H. Jaeger (1946) *Dermatologica*, 92, 325.

In the present case the diagnosis of chronic rheumatic nodules would seem more likely than granuloma annulare. The object in presenting it is to emphasize the histological similarity of the two conditions, and even a certain clinical resemblance. Is it possible that they are related in some way?

Dr. F. Parkes Weber: The histology of the large elbow nodule is certainly that of the typical necrobiotic nodules of rheumatoid arthritis, and, in fact, the patient's fingers resemble those of not very active and not far advanced rheumatoid arthritis.

Dr. G. B. Dowling: About six weeks ago a doctor of 57 saw me for a ringed lesion over two knuckles on the right hand. This he had diagnosed himself as granuloma annulare, but, oddly enough, he did not connect the ringed lesion on the hand with a far more striking lesion on the left elbow. This, a firm subcutaneous tumour-like swelling, began to develop over the posterior border of the left ulna a little below the elbow about two years ago; shortly afterwards a plaque appeared on the back of the right hand which spread, gradually becoming ringed.

He had sciatica three years ago followed later by swelling of fingers and pain in the lower back muscles. Mild degree of pain in muscles and joints persisted.

He exhibited on the back of the right hand a ringed nodular lesion centred by the knuckles of the first and second fingers; on the extensor aspect of the left forearm about an inch below the elbow a subcutaneous tumour-like lesion, freely movable under the skin and over the underlying bone. It felt like a lobulated mass of small firm tumours. Slight swelling of one or two finger-joints was present.

The case is similar in every respect to that presented by Dr. Bowers except that there is one lesion less and the patient shows less rheumatic change.

I was personally unaware that any histological similarity between granuloma annulare and the rheumatic nodule was known to exist. However, Dr. Bowers pointed out to me that this was so, and it was brought home to me again by Dr. Haber in connexion with a third case of the same kind

0.5% novocain solution which interrupts afferent paths without interfering with the motor paths.

Upstream of the anterior horn cells, pyramidal and cerebral affections as well as proprioceptive impulses from collateral afferent paths can mediate the responses of the anterior horn cells or elicit reflex action, so that electrical activity coupled with clinical rigidity may result. In affections of the basal ganglia—such as Parkinsonism—rhythmic surges can be obtained.

I do not anticipate that E.M.G. will for some time to come be used in the same way as radiography, electrocardiography or electro-encephalography, where an operator carries out the technical aspect of the investigation and submits a record for interpretation to a clinician.

It is, in the case of E.M.G., too important to observe the patient personally during the actual examination and, if necessary, to modify the conditions under which the examination is conducted.

It may well be possible in future to standardize recording technique and terminology to such an extent as to make this practicable but the time has not yet come.

I feel that this clinical application of electrophysiology has great potentialities but that the value of the contribution which it may ultimately bring to neurology will in a large measure depend on how well it is supported during its developmental stages by the tripod made of the neurologist, the neurosurgeon and the morbid pathologist.

Each of these can confirm or reject a tentative diagnosis either on clinical grounds or as the result of an exploration or a biopsy.

Dr. Graham Weddell was the pioneer worker in this field. In collaboration with Feinstein and Pattle he investigated a number of conditions presenting interesting electromyographic features. By overcoming some of the technical difficulties which had prevented electromyography from emerging from the laboratory they put it at the disposal of the clinician.

I also wish to pay a tribute to Mr. Peter Styles whose ability has made further technical developments clinically accessible.

Dr. Graham Weddell said that electromyography was not only a valuable aid to diagnosis but was of importance also in relation to the physiology of muscular contraction. Dr. Weddell stated that he and his colleagues were particularly interested in the total pattern of innervation of a voluntary muscle and were planning to correlate anatomical findings with the results of action potential recordings. In his department Dr. W. H. Feindel had developed a new staining technique using methylene-blue, by means of which it is possible to study the innervation of an entire muscle without the distortion consequent upon local injection of the dye. It was proving of extreme value in this connexion. Dr. Weddell showed a number of slides illustrating some of the details of the pattern of innervation of muscle upon which he and his colleagues were at present engaged. He pointed out the value of making electromyographical studies in disease processes involving the muscular and nervous systems, as Dr. Bauwens was doing, for pathological lesions often perform physiological experiments of a slowly progressive nature, which are difficult to reproduce in the laboratory.

- (4) With the diminution of the seborrhœa, the hair of the scalp becomes drier and "fluffy", as in the normal or pregnant female.
- (5) Dandruff ceases to form and may disappear without local treatment of the scalp.
- (6) The comedones shrivel, become desiccated, and may easily be picked out of the follicles with the finger-nail.
- (7) Pustules subside, and the indurated and cystic lesions gradually involute.
- (8) The growth of coarse hair on the face diminishes in vigour, so that daily shaving may be hardly necessary.

The patients, of course, develop a varying degree of gynæcomastia. The areolæ of the nipples become deeply pigmented, and on their surfaces may be seen droplets of sweat from the apocrine glands. All libido ceases, and disinclination for physical or mental activity may result. Return to normal, however, occurs rapidly after removal of the pellets. The acne may then relapse to some extent, but in my experience never seriously.

The possible effect of the treatment on spermatogenesis is a matter of obvious importance. Dr. Bishop has done sperm-counts in a few cases and they were normal, but we are both reluctant to advise this treatment except in cases in which severe disfigurement is likely to result from the acne, and in acne conglobata.

Dr. C. H. Whittle: Was there any evidence of tuberculosis in this case? I had a similar case in a thin, weedy man aged 40, whose buttocks were riddled with abscesses and sinuses for years. The infecting organism appeared to be a golden staphylococcus; but when portions of the lesions were removed at post-mortem, following his death from pneumonia, the sections showed a tuberculous structure with acid-alcohol-fast bacilli present.

Dr. Louis Forman: Before the implant the hair on the face was stiff and adult. It disappeared from the face while the implant was being absorbed, and has since grown again but is soft and fluffy.

The abscesses were examined bacteriologically. The acne bacillus and *Staphylococcus albus* were grown. No moulds were grown from the pus. Examination of the pus and of part of the wall of one of the abscesses revealed no evidence of tuberculosis.

Subcutaneous Nodules: For Diagnosis. ? Granuloma Annulare.—J. P. M. TIZARD, M.R.C.P. (for Professor A. A. MONCRIEFF).

W. H., female, aged 3 years 4 months. Perfectly well until April 1947, when lumps on the back of the head were noticed. Two weeks later two more lumps appeared in the palm of the right hand. The child did not complain of pain or discomfort. In June 1947, she appeared well, normal height but slightly underweight. Tonsils somewhat enlarged, but not infected. Small glands palpable in the neck and axillæ. Four nodules palpable in the left occipital region, one below the right axilla and two on the radial side of the right palm. A faint, circinate rash consisting of pale, pin-head papules was noticed on the abdominal wall (this has disappeared since). Thyroid slightly enlarged. No other abnormal clinical findings.

While in hospital for one week she was afebrile and there was no tachycardia. Red cell count 4,620,000. White cells 8,800 per c.mm. Eosinos. 5%. B.S.R. 7 mm. in one hour. X-rays: No evidence of calcification in the nodules; lung fields clear; heart—slight prominence in the region of the conus.

Biopsy report on one scalp nodule and the axillary nodule (Dr. M. Bodian).—The peripheral portion (fig. 1) of each nodule showed a large number of new capillaries and mainly perivascular collections of large rounded and elongated mononuclear cells as well as lymphocytes. Many of the mononuclear cells showed pyknotic nuclei with some mitotic figures, and there were a number of bi- and tri-nucleated cells present, but no large foreign-body giant-cell types. The central core of the nodule was much less vascular, and showed a definitely nodular arrangement of cells of similar types as above mentioned, as well as an increasing number of fibroblasts. Each nodule showed a degenerated central portion with few ghost-like cells and myxomatous and fibrinoid intercellular material (fig. 2). One of the degenerated areas contained a fair number of eosinophil leucocytes. The nearer the centre, the more collagen was laid down by the fibroblasts which in parts underwent myxomatous or fibrinoid degeneration (fig. 3). Nervous elements could not be found.

The general impression is of a very actively growing granulomatous lesion in the most peripheral or recently developed portions, and more fibrosis and degeneration in the more central or older parts of the nodule. These features indicate an allergic lesion, somewhat reminiscent of a rheumatic nodule.

Progress.—The nodules have increased slightly in size, and fresh nodules have appeared over the sixth and twelfth dorsal spines; at the junction of the sixth right costal cartilage and sternum and two additional nodules in the left occipital region. The nodules are about $\frac{1}{2}$ in. in diameter and are firm and painless. With the exception of those in the scalp and palm, the overlying skin is freely movable, but the nodules appear to be attached deeply. The child is still in good health; no evidence of carditis; eye examination, fundi and media normal; afebrile; hæmoglobin 96%; white cells 6,200, 1% eosinophils; B.S.R. 3 mm. in one hour; Blood Wassermann and Kahn reactions, negative; Mantoux 1/1,000, negative.

which I saw at St. John's Hospital. A section of one of the lesions in this case showed changes which were characteristic of granuloma annulare but Dr. Haber remarked in his report that they might equally be found in the nodules of rheumatoid arthritis. This patient had lesions on the forearms and fingers. Unfortunately, I saw her only once and omitted to ask her whether she suffered from rheumatism or not.

Both the case shown to-day and my case have lesions which are characteristic of rheumatic nodules, and each has one which is clinically suggestive of granuloma annulare.

These two facts, namely, histological and clinical similarity, do appear to point to the possibility of a common factor. There is, in addition, a characteristic third similar feature, that of distribution over bony prominences.

Dr. F. Parkes Weber: The similarity in the microscopic features of granuloma annulare and the necrobiotic nodules of rheumatoid arthritis, which was generally supposed to be unrelated by aetiology, is made more confusing still by a case like this important one of Dr. Dowling's.

Dr. A. C. Roxburgh: In 1936 I showed three cases of granuloma annulare at the meeting of the British Association of Dermatology (*Brit. J. Derm.*, 48, 633). One was typical, but one of the others had lesions on the elbows exactly the same as in Dr. Bowers' case and apparently also that of Dr. Dowling's, and they were diagnosed on the strength of the section as being granuloma annulare.

Acne Conglobata treated by Implantation of 300 mg. of Stilbæstrol.—**L. FORMAN, M.D.**

W. W., male, aged 21. (Previously shown at the meeting of the Section on March 20, 1947. *Proc. R. Soc. Med.*, 40, 699.)

At the age of 16 years he was six feet tall, plump, with well-developed genitalia and hair growth of the face and limbs. The skin of the face, chest and back was intensely seborrhœic with comedones, acne pustules and abscesses. In the armpits and perianal area, large deep abscesses communicated with each other, leaving epithelial bridges, and granulating, pus-covered ridges. The buttocks and perianal skin were grossly involved and indurated with subcutaneous abscesses and numerous sinuses.

Four years' continuous local treatment and general measures for his severe anæmia (Hb. 60%) led to some improvement.

In May 1947, Dr. Peter Bishop implanted 300 mg. of stilbæstrol, and to-day the effects of this treatment are to be seen. The skin of the face has become fine and delicate, and is no longer seborrhœic. The abscesses of the axillæ and perianal area are fewer, and the skin in these regions is less indurated. The breasts are enlarged, the external genitalia smaller, and he has lost his libido.

The pellet of œstrogen has probably been largely absorbed by this time, as is shown by the regrowth of fine, fluffy hair on the face. The areolæ of the breasts had become diffusely pigmented, but this pigment is now seen as patchy brown areas in the superficial layers of the epidermis, and is being desquamated.

Another interesting manifestation of the declining activity of the œstrogen is the flushing of his face, which was noticeable during the past month. He himself has been aware of this flushing particularly during the afternoon—a symptom comparable to menopausal flushing.

In this patient the effects of implanted œstrogens are observed—namely breast enlargement, shrinkage of the penis and probably the testicles, diminution in activity and size of sebaceous glands, and refinement and feminization of the skin. Œstrogen implant was suggested because of the severity of the disease although the reversal of the sexuality over a period of six to nine months is undesirable. Again it is known from experiments on rats that the germinal epithelium of the testes suffers severely. As far as I know sperm counts have not been carried out over the period of implant to determine if any permanent damage occurs in man treated with œstrogen implants.

However, this patient had been under constant treatment for four years, with periods up to a year in hospital. He was unable to work, and was showing the toxic effects of long-standing and extensive skin sepsis. At one time it was suggested that he might develop amyloidosis, for he lost a good deal of weight, developed an anæmia of 60% hæmoglobin and was going downhill.

Dr. H. W. Barber: I have had considerable experience of this method of treatment. In one case of acne conglobata, in whom the condition had been present many years and was associated with the so-called acne keloid on the neck and occipital region, the lesions in the groins and on the buttocks were very similar to those in Dr. Forman's case, and the constantly recurring deep abscesses made his life almost unbearable.

Subcutaneous implantation of stilbæstrol by Dr. Peter Bishop was followed by complete involution of the whole condition. Removal of the pellets was followed by some degree of relapse, but his condition was satisfactory when he was last seen.

Dr. Bishop has treated several cases of severe cystic acne for me by the same method. The effects on the skin may be summarized as follows:

- (1) The activity of the sebaceous glands is remarkably diminished.
- (2) The pilo-sebaceous orifices are reduced in size and are no longer easily visible to the naked eye.
- (3) The slight hypertrophy of the stratum corneum disappears, and the surface of the skin becomes smooth and delicate, like that of a child.

Dr. J. P. M. Tizard (in reply to a question): We have considered rheumatism very unlikely in view of the child's age, but we intend to keep her under observation.

POSTSCRIPT.—Dr. Dowling's remarks seem to provide the clue to the nature of these nodules, which are apparently the subcutaneous form of granuloma annulare.

A case, strikingly similar in its clinical and pathological aspects, was described by Grauer in 1934 (*Arch. Derm. Syph.*, 30, 785).

The following cases were also shown:

Acute Lichen Planus.—Dr. C. D. CALNAN (for Dr. I. MUENDE).

Necrobiosis Lipoidica (Sine Diabetes).—Dr. RONALD SCUTT (for Dr. J. L. FRANKLIN).

Erythrodermia Congenitale Ichthyosiforme.—Dr. G. B. MITCHELL-HEGGS and Dr. M. FEIWEL.

Mycosis Fungoides à Tumeurs d'Emblée.—Dr. C. H. WHITTLE.

? Pityriasis Rubra Pilaris. ? Darier's Disease.—Dr. R. M. B. MACKENNA and Dr. BERNARD GREEN.

Urticaria Pigmentosa.—Dr. F. R. BETTLEY.

(1) Epidermodysplasia Verruciformis (Lutz and Lewandowsky). ? Plane Warts resembling Lichen Planus Chronicus. (2) Acrodermatitis Chronica 'Atrophicans' (Herxheimer and Hartmann) (Presented as ? Berlock Dermatitis).—Dr. BRIAN RUSSELL.

(These cases may be published later in the *British Journal of Dermatology*.)

[January 15, 1948]

Histiocytoma.—ALICE CARLETON, M.D.

A healthy young woman has during the past six years, developed six small tumours on the thighs and upper arms. Each has followed an insect bite. The individual tumours are round, smooth and hard, brownish red in colour, and sharply defined on palpation. They grow slowly to a size of about 1.5 cm. and then remain stationary. No subjective sensation is felt. There is no family history of diabetes.

Senear, F. E., and Caro, M. R., 1936, *Arch. Derm. Syph.*, Chicago, 33, 209, reviewing 25 cases, found no significant connexion with sex or age. The usual site was the upper part of the limbs. Several followed minor injuries such as insect bites. They are usually single, only 4 out of 25 being multiple.

Arnold, L., and Tilden, I. L., 1943, *Arch. Derm. Syph. Chicago*, 47, 498, found a family history of diabetes in 50%.

The Chairman (Dr. A. C. Roxburgh): What is the best treatment?

Dr. Carleton: Excision.

Dr. F. F. Hillier : The histiocytoma was originally described by Pautrier and Woringer (1933, *Bull. Soc. franç. Derm. Syph.*, 40, 1659) who demonstrated the presence of fat and other bodies in the cells of many so-called fibromata; this phagocytic power showed that the essential cell was a histiocyte and not a fibroblast. I believe that one cannot differentiate absolutely between these two types of cell. The fibroblast, especially in the more primitive form found in tumours, given adequate stimuli may regain properties which it has lost in becoming specialized. Thus the primitive fibroblast may be capable of phagocytosis and be indistinguishable from the primitive histiocyte.

Four Cases by BRIAN RUSSELL, M.D.

Case I.—Dermatitis (Flavine) treated with Large Daily Doses of Crude Liver.

S. M., male, aged 41.

History.—1943: He received a severe wound, 8 in. by $\frac{1}{2}$ in., on the ulnar aspect of the left forearm. It was treated with sulphonamide powder. After four days he developed a rash which persisted for five months.

1947: He grazed his buttock and it was treated with flavine dressings. Cellulitis of the right thigh developed, and was treated with penicillin injections.

A symmetrical, follicular, crusted eruption appeared on his face, arms, legs and trunk.

Treatment.—Crude liver injections, 2 ml. daily for six days; and calamine lotion.

In less than a week the condition resolved leaving scaling erythematous remnants.

Then a slight follicular, papular recurrence was noted around the edge of the primary lesion and a few discrete papules on the forearms. A further injection of 4 ml. crude liver was given and the condition resolved.

Case II.—Seborrhæic Dermatitis with Exacerbation from Acriflavine.

M. B., female, aged 43.

History.—1938: She had "dermatitis" all over the body. She has had recurrences since at times of worry.

Dr. G. B. Dowling: An interesting feature of this case is the lesion of the palm and the question whether it is granuloma annulare. It has a whitish, papular, nodular appearance, whereas the other lesions are subcutaneous.

Dr. F. Parkes Weber: On the whole, the case seems to be one of "rheumatismus nodosus" of a chronic type, without as yet any articular rheumatism or cardiac involvement. The nodules in the occipital region are, clinically, especially characteristic. An interesting point is that microscopical



FIG. 1.— $\times 150$. Hæmatoxylin eosin.

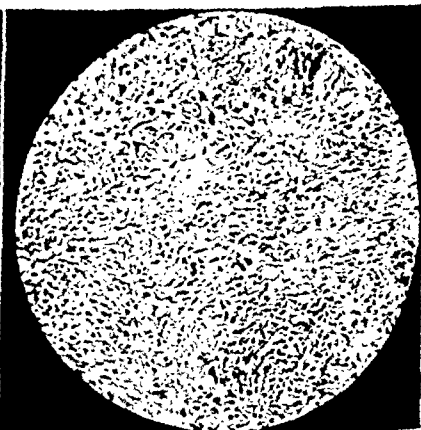


FIG. 2.— $\times 63$. Hæmatoxylin eosin.

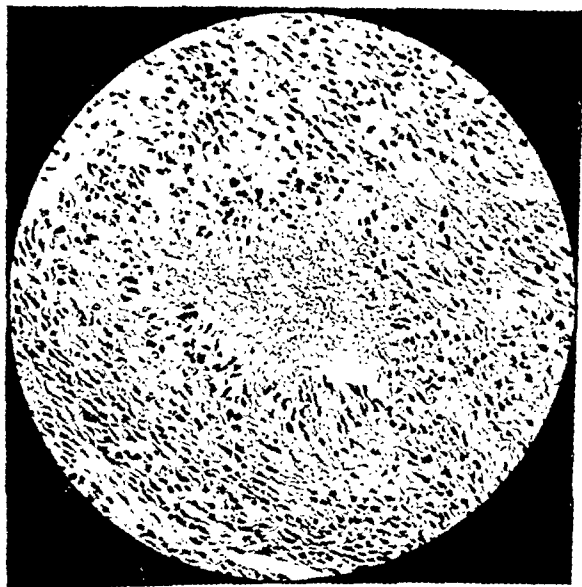


FIG. 3.— $\times 145$. Hæmatoxylin eosin.

FIG. 1.—Peripheral portion of a nodule showing a perivascular collection of large rounded and elongated mononuclear cells and lymphocytes.

FIG. 2.—A portion of a nodule showing the fibrinoid intercellular substance.

FIG. 3.—Higher power view showing radiation of fibroblasts round the central zone of degeneration.

examination of one of the lesions suggests at one part a necrobiotic nodule of rheumatoid arthritis. (The palmar nodules are an unusual, remarkable feature.)

Dr. R. E. Bowers: Coates and Coombs, in a paper on rheumatic nodules (*Arch. Dis. Childh.*, 1926, 1, 183), mention the occasional occurrence of multiple small subcutaneous "granules"; they conclude them to be of rheumatic origin, but say that they do not necessarily indicate a severe cardiac lesion.

Histologically, it may be difficult to differentiate an ageing nodule of acute rheumatism from that of chronic rheumatoid arthritis: both are sometimes indistinguishable from granuloma annulare.

Dr. F. Parkes Weber: It is imperative to keep this child for years under observation. The condition may be one in which the heart ultimately becomes involved.

Comment.—These cases are presented to show the value of daily high intramuscular dosage with crude liver extract in the treatment of sulphonamide and flavine dermatitis complicated by a generalized sensitization dermatitis. This condition tends to develop, as Gottschalk, H. R., and Weiss, R. S. (1947, *Arch. Derm. Syph., Chicago*, 56, 775), have observed with sulphonamides, when these substances, or flavine, are applied over relatively large areas of skin and particularly on damaged skin, and it seems to be necessary for a contact dermatitis from these agents to attain a certain critical size before generalized sensitization occurs.

The dermatoses produced by sulphonamides and flavine are very similar, if not identical, and other substances that can cause widespread sensitization with exudation include mercurials and paraphenylenediamine. With penicillin, a longer period of contact is usual before the development of sensitization, which also tends to be less severe and more localized.

Treatment by injection of liver, recommended as a routine procedure as a detoxifying measure in sulphonamide dermatitis by Abramowitz, E. W. (1944, *Arch. Derm. Syph., Chicago*, 50, 289), has been used in 33 consecutive cases of sensitization dermatitis from known causes, with the following results:

	Number of cases	Cleared 1-6 weeks (average 3 weeks)	Marked improvement 1-7 weeks (average 3½ weeks)	Slight improvement 2-3 weeks
Flavine	7	6	1	0
Sulphonamide .. .	7	6	1	0
Flavine and Sulphonamide .. .	3	3	0	0
Ammoniated mercury .. .	5	4	1	0
Paraphenylenediamine .. .	2	1	1	0
Penicillin	9	3	4	2

A control group has not been studied so that it is not possible to say how long these cases would have taken to resolve if treated in a different manner.

These figures refer to the secondary sensitization dermatitis. The primary lesions improve more slowly but also become dry, pale and scaly. Minor relapses after stopping treatment have also responded but results have been much less uniform with penicillin.

It is suggested that these conditions may represent states of disturbed metabolism from impairment of liver function arising from the absorption from extensive moist areas of substances known to be hepatotoxic. Breakdown products of cells and bacteria may also play a part ("autolytic eczema"), and Hartmann, F. W., and Romence, H. L. (1943, *Ann. Surg.*, 118, 402), noticed that in the treatment of burns in dogs, the use of wet dressings of tannic acid, silver nitrate, or ferric chloride, gave the highest incidence of liver degeneration or necrosis, and that degenerative changes even occurred after saline dressings. Dry applications of these agents were much less harmful.

The Chairman (Dr. A. C. Roxburgh): We know only too well the unfortunate results of the continued application of sulphonamides to the skin, but it is difficult to say anyone, other than a dermatologist, to realize the danger. Another point is that acriflavine aggravates sulphonamide dermatitis very severely. I am glad to learn that crude liver extract is so helpful because some of these cases are very resistant to treatment.

Dr. Louis Forman: Sensitization to antibiotics and antiseptics applied to the skin giving rise to a general eczematous dermatitis has been of frequent occurrence. The case of acriflavine dermatitis which responded so well to liver injections impressed me because in my experience a generalized dermatitis due to acriflavine runs a very prolonged course.

Dr. Russell believes that liver function may be disturbed in these cases of generalized dermatitis. However, it is possible that the epidermal cells when widely inflamed may not be able to absorb available vitamins in the amount normally present, or the demands may be greater. We know that extra vitamin C is required when there is widespread tissue inflammation.

The injections of liver may have supplied the skin with the increased amount of vitamin-B group which is needed by the epidermal cells.

I have had cases of exudative and lichenified dermatitis occurring on the scalp, face and elsewhere associated with evidence of gastro-intestinal disease, e.g. gastric or duodenal ulcer and Crohn's disease.

One old man with a fatty diarrhoea had extensive areas of lichenified dermatitis on the trunk and limbs. He had a severe high colour-index anaemia. There was no reticulocyte response to liver by injection so that it was not a true pernicious anaemia. However, plexan 2 ml. given daily produced a remarkable improvement in the skin condition. He remained well on monthly injections and then was put on to folic acid by mouth, the injections being stopped. It was hoped the folic acid by mouth would increase the absorption of vitamin-B group from the gut but he relapsed with papular lesions on the sites of the old areas of lichenification.

Dr. E. J. Moynahan: I wonder whether Dr. Brian Russell has any real evidence of interference with liver function. It is difficult to believe that substances as different as penicillin, acriflavine and

February 1947: Following a kick, she developed an ulcer on the ankle which has not healed since. The ulcer has been treated with penicillin ointment; adhesive bandages; cod-liver oil; and acriflavine, which helped at first but was then followed by profuse exudation.

On examination (17.12.47).—Marked pityriasis capitis. There was a seborrhœic type of eczema on the neck, upper lip, sternum, axillæ, antecubital areas, popliteal regions, and groins.

Treatment.—She was given injections of plexan 2 ml. twice weekly for one month; then once weekly for two weeks. Calamine liniment with ichthylol was also given.

She felt much better after the first injection and the bowels were more regular. The eruption became dry in one week. 31.12.47: There were faint, scaling remnants. She was to continue with vitamin B complex, or liver by mouth.

Case III.—Dermatitis (Sulphonamide) Treated with Large Daily Doses of Crude Liver.

R. K., male, aged 57.

History.—In 1947 he received a lacerated wound on the back of the left forearm just below the elbow. It was treated with penicillin powder (with sulphathiazole) and eusol.

An exuding rash developed around wound, spreading to the scrotum, calves, face, head and neck.

On examination.—There was a patchy, crusted erythema of the beard, in follicular pattern. A moist erythema for 2 in. around the wound, below the left elbow, with outlying follicular pustules. Peeling of the tongue, in geographical pattern. Scaling and œdema of the scrotum. Patchy, follicular, crusted erythema of the legs, and confluent behind the left knee.

Treatment.—Injections of plexan 2 ml. daily for six days, and calamine liniment.

In one week there was a striking improvement. All lesions were dry and subsiding. Face was almost clear; tongue clear. Two further injections of plexan 2 ml. were given in the next week.

Shortly afterwards he developed three furuncles on the knee. His doctor gave sulphonamide tablets, one twice a day. There was a severe recurrence. Face, head, forearms, and site of injury all exuded profusely again. The tongue became furred. He was given plexan injections 2 ml. daily for four days, after the second of which the skin was again dry. The tongue showed geographical areas of denudation: scaly remnants only in groin, and three resolving boils right inner knee. He was given calamine lotion.

After a week's improvement a slight tendency to relapse was noted on the forearms, with scaling patches. Plexan injections 2 ml. were given three times a week. These were continued for three weeks by which time the face was normal and the forearms and thighs were faintly scaling and pink.

Case IV.—Dermatitis (Flavine) Treated with Large Daily Doses of Crude Liver.

L. S., male, aged 33.

History.—In 1945 he received severe petrol burns on the face, arms, body and legs, when serving in the Middle East. He was treated with saline and acriflavine for ten days, without detriment, and the burns healed.

For eighteen months he has had a few spots and exudation behind the right knee, which he has treated with calamine lotion, but on one occasion he applied acriflavine. Shortly afterwards he developed a rash on the body, and has been attending hospital since, having various treatments; a patent ointment on one occasion aggravated the rash.

He then applied a dry yellow Army dressing to the back of the knee. The next day there was profuse exudation and, six days after the application, the rash spread to his face.

On examination.—Nervous and apprehensive. There was a golden-crusted, follicular erythema over the whole face and neck; a confluent, marginally follicular, crusted, exuding erythema of forearms; a confluent, exuding erythema in both popliteal spaces; a disseminated, discrete, follicular erythema on the trunk and the rest of the limbs; pompholyx of the hands. The tongue and mucosæ were normal.

Treatment.—4–5 ml. plexan daily for one week. Calamine liniment was applied to the lesions and light gauze dressings to the limbs.

After six days of treatment, the lesions on the face were all dry. The primary lesion behind the right knee was almost dry. The confluent, exuding erythema of the forearms had formed dry, golden crusts which were not disturbed but merely covered with a dry dressing which was removed a few days later, leaving a normal, dry, scaling surface beneath.

Progress.—When the face was quite clear and the forearms and legs much improved the dosage of plexan was reduced to 2 ml. daily.

When last seen the face was quite clear. There were dry, follicular papules, without erythema, on the forearms. The right popliteal space was dry and crusted in a small area.

treatment: ferrous sulphate gr. 3 b.d. and yeast extract gr. 5 with each dose of sulphetrone.

Progress.—Ulcer healing rapidly. Nasal swab: *My. lepræ* still present but in very small numbers.



FIG. 1.—Taken a few days after the commencement of treatment with sulphetrone.



FIG. 2.—Taken two months after the commencement of treatment with sulphetrone.

Blood-counts:—

	Before Treatment 2.1.48	During Treatment 15.1.48
Red blood cells ..	4,850,000	4,650,000
Hæmoglobin ..	97%	88%
Colour-index ..	1.0	0.94
White blood cells	14,000	14,800
Polymorphs ..	68%	59%
Eosinophils ..	—	2%
Basophils ..	—	2%
Lymphocytes ..	33%	33%
Monocytes ..	2%	4%

Biopsy (Dr. I. Muende).—There are numerous foci of dense collagen bundles among which there are many pale vacuolated fibroblasts. Between these foci there is a dense cellular infiltration composed of plasma cells, lymphoid cells and pale endothelial cells. In the superficial ulcerated area the vessels are dilated and engorged and surrounded by numerous polymorphs and lymphoid cells. Ziehl-Neelsen preparations show the presence of numerous acid-fast bacilli.

The following cases were also shown:

Multiple Idiopathic Hæmorrhagic Pigmented Sarcoma (Kaposi).—Dr. M. SKOBLO (for Dr. J. E. M. WIGLEY).

Two Cases of Necrobiosis Lipoidica Diabeticorum.—Dr. G. B. MITCHELL-HEGGS and Dr. M. FEIWEL.

(These cases may be published later in the *British Journal of Dermatology*.)

[February 19, 1948]

Pustular Eruption: for Diagnosis.—J. R. SIMPSON, M.B., M.R.C.P.

Mr. R. R., aged 59, a farmer.

History.—For the last four and a half years he has had an itching, pustular rash affecting the trunk, the lower part of the neck and the proximal parts of the limbs. The rash has not changed in its essential features, although it has waxed and waned, for no apparent reason, and he has had several almost complete remissions lasting for two or three weeks. He has

the sulphonamides can be responsible in the way he has suggested. It is also erroneous to draw conclusions from what happens to the liver in animals, because animals respond in a different way. Skin irritants have been shown to have an effect more on the stomach than on the liver. Finally, liver extract is not of much value in the treatment of hepatitis, except by way of vitamin supplement.

Dr. Brian Russell: In reply to Dr. Moynahan, in my opinion tests of liver function are so insensitive as to be of little value. A liver puncture would give the information required but I do not consider the risk is justified, particularly as flavine and sulphonamides are known to be absorbed, for example, from burns, and have been reported to cause liver damage and even necrosis. Regarding penicillin sensitivity, I would suggest that there is an increasing number of individuals who have been sensitized by the use of sulphonamides and flavine, so that they suffer from a subclinical hepatic insufficiency and react unfavourably to relatively milder agents.

Dr. R. M. B. MacKenna: Acriflavine before the war was usually considered a safe application, and now we regard it as a fairly dangerous one. The incidence of dermatitis caused by weak alkalis, particularly on the hands of middle-class women, seems to be rising, and our skin resistance to these relatively innocuous chemicals seems to be dropping. If this is so it is a serious matter for the community as a whole. In one of the cases exhibited to-day the patient told me that when there was a flare-up he applied a dry military dressing which he said contained acriflavine. I asked him why he thought it contained acriflavine, and he replied that it was because it was yellow; but it might equally have contained picric acid, which will provoke a similar eruption and a rather more severe one.

Dr. G. B. Mitchell-Heggs: Before we accept this thesis *in toto*, we should bear in mind similar cases which have benefited in a dramatic fashion by injections of other foreign proteins.

I gather that the liver has to be severely damaged before this can be detected by liver tolerance tests or be improved by parenteral liver extract therapy.

Cirrhosis of the liver is now rather uncommon. When I was a student it was more common, but I only recall a few who were having treatment for a skin condition. In addition I have seen similar cases of seborrhœic dermatitis respond to vaccine therapy and the elimination of septic foci and chronic anxiety.

We are seeing more patients to-day suffering from conditions of the skin, which are in some way associated with deficiencies in diet. One finds that many improve on an increase of vitamins A, B-complex and D.

Dr. F. F. Hellier: Before we accept these results we must be careful that there are not other factors playing a part, such as the effect of admission to hospital which, at least in one case, occurred synchronously with the commencement of the injections; one must also allow for the enthusiasm of the dermatologist, which has a good effect on the patient whatever he does for him. I saw, as many of us did during the war, an enormous amount of resistant sulphonamide dermatitis, and yet it could not be said that our soldiers were ever short of food or vitamins. Indeed, they had never been better fed in their lives. Therefore I do not think that shortage of food can be the cause of either the supposed increased incidence or resistance of cases of dermatitis. Nowadays more people are exposed to chemotherapeutic substances than before the war, when not many of these synthetic preparations were available. We see more housewives now suffering from dermatitis for the simple reason that the modern housewife, if she gets a dermatitis, can no longer find a neighbour to do her washing. Before the war there were various ways by which she could avoid any work which irritated her condition but now she has to carry on as best she can; in addition she is exposed to many new chemicals capable of producing dermatitis.

One sees a lot of penicillin dermatitis nowadays, and yet in the first two years during which penicillin was used in the country we hardly saw any at all. I do not know what the explanation is, whether it is some alteration in the penicillin or in the base, but I do not think it can be attributed to deficiency of diet as the same thing is happening in America.

Dr. Brian Russell: I may be too hopeful about these cases, but some of the patients describe relief from depression, anorexia, and constipation, in addition to the improvement in the skin condition. The continued improvement is far in excess of that noted after the use of T.A.B.

In reply to Dr. Hellier, I confess the treatment has been given with enthusiasm, but the treatment of the first case was carried out by Dr. A. J. Nicholas, who, following his experience of conditions of malnutrition in Burma, employed a much higher dose than we were giving at that time. Only 8 of the 33 cases were treated as in-patients.

Leprosy.—A. I. SUCHETT-KAYE, M.D. (for A. H. HARKNESS, M.R.C.S.).

A Chinese seaman, aged 41, with a history of syphilis two years previously, was sent to the V.D. Dept. of St. Peter's Hospital (9.12.47) with a diagnosis of gumma. The previous history showed that two weeks before admission a gangrenous-looking vesicle appeared just below and on the anterior aspect of the left knee and when first seen it had developed into a deep punched-out ulcer, 2 in. by 2½ in. Scrapings from both the ulcer and nasopharynx were positive for *My. lepre* and negative for *S. pallida*, Vincent's organisms, Ducrey's bacilli, Leishman-Donovan bodies and *C. diphtheriæ*.

Central nervous system.—Paræsthesia involving the facial nerves. Sensory loss to pin-prick corresponding to C6, C7, C8, L4 and L5. C.S.F. normal.

Treatment.—Sulphetrone (B.W. & Co.) 1 gramme six-hourly by mouth. Blood levels, carried out by Dr. G. Brownlee on two occasions, were 3.0 mg. per 100 ml. Adjuvant

treatment: ferrous sulphate gr. 3 b.d. and yeast extract gr. 5 with each dose of sulphetrone.

Progress.—Ulcer healing rapidly. Nasal swab: *My. lepræ* still present but in very small numbers.



FIG. 1.—Taken a few days after the commencement of treatment with sulphetrone.



FIG. 2.—Taken two months after the commencement of treatment with sulphetrone.

Blood-counts:—

	Before Treatment 2.1.48	During Treatment 15.1.48
Red blood cells ..	4,850,000	4,650,000
Hæmoglobin ..	97%	88%
Colour-index ..	1.0	0.94
White blood cells	14,000	14,800
Polymorphs ..	68%	59%
Eosinophils ..	—	2%
Basophils ..	—	2%
Lymphocytes ..	33%	33%
Monocytes ..	2%	4%

Biopsy (Dr. I. Muende).—There are numerous foci of dense collagen bundles among which there are many pale vacuolated fibroblasts. Between these foci there is a dense cellular infiltration composed of plasma cells, lymphoid cells and pale endothelial cells. In the superficial ulcerated area the vessels are dilated and engorged and surrounded by numerous polymorphs and lymphoid cells. Ziehl-Neelsen preparations show the presence of numerous acid-fast bacilli.

The following cases were also shown:

Multiple Idiopathic Hæmorrhagic Pigmented Sarcoma (Kaposi).—Dr. M. SKOBLO (for Dr. J. E. M. WIGLEY).

Two Cases of Necrobiosis Lipoidica Diabeticorum.—Dr. G. B. MITCHELL-HEGGS and Dr. M. FEIWEL.

(These cases may be published later in the *British Journal of Dermatology*.)

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Mr. R. R., aged 59, a farmer.

History.—For the last four and a half years he has had an itching, pustular rash affecting the trunk, the lower part of the neck and the proximal parts of the limbs. The rash has not changed in its essential features, although it has waxed and waned, for no apparent reason, and he has had several almost complete remissions lasting for two or three weeks. He has

not been taking patent medicines. Erysipelas of the face twenty years ago. Right inguinal hernia and varicocele treated surgically in 1945.

On examination.—The eruption is symmetrical. It is most profuse on the whole of the trunk, but is also present on the lower part of the neck, the shoulders, the upper half of the arms and on the thighs; the buttocks and the sacral and olecranon areas being spared. It is composed chiefly of pustules, 2 to 4 mm. in diameter, each with an erythematous halo, and red macules covered with yellow scales and crusts. A few clear vesicles surrounded by normal skin can also be seen. The lesions are grouped in some places, but do not all show the same stage of development in any one area.

He is edentulous and no abnormality was found in the heart, lungs, abdomen, or central nervous system.

Investigations.

Blood-count normal.

Contents of pustule.—Gram film: No organisms seen. Leishman film: Neutros. 98.5%; lymphos. 1.0%; eosinos. 0.5%.

Cultures (blood-trypsin-agar) sterile after forty-eight hours.

Mantoux reaction negative—1:1000. Wassermann and Kahn reactions negative.

Biopsy.—Section shows oedema of the epidermis and a vesicle containing polymorphs beneath the stratum corneum. There is a scanty leucocytic infiltration of the epidermis and corium. There is no preponderance of eosinophils.

X-rays: Chest—nothing abnormal. Nasal sinuses: mucosal thickening of both antra and a polypus in the left antrum.

Tonsillar swab.—Streptococci, viridans type: light growth. *M. catarrhalis*: moderate growth. No hæmolytic streptococci or diphtheria bacilli grown.

30.12.47: Bilateral antral puncture and wash-out with evacuation of mucopus (Mr. Phillip Scott). This was repeated twice without finding pus and no further treatment advised for the nose.

Treatment has also included sulphapyridine 0.5 gramme t.i.d. for seven weeks and liq. arsenicalis minims 5 t.i.d. for two weeks; these had no effect on the rash.

Dr. P. J. Feeny: Now that more success is being obtained in culturing viruses, I wonder if one should seriously consider culturing cerebrospinal fluid from this type of case and from cases of pemphigus and dermatitis herpetiformis with a view to locating a possible virus.

Dr. W. Lemberger: Since 1872 when impetigo herpetiformis was first described many atypical cases taking a less malignant course have been reported. If one is prepared to regard this case as belonging to this group of pustular eruptions one would have to remember from the therapeutic point of view that in some cases a definite endocrine relationship appears to exist. I am referring to cases with signs of hypoparathyroidism in which dihydrotachysterol, A.T.10, proved helpful.

Dr. Ivan H. McCaw: I have been looking after a boy of 10 who has a condition very similar to this. He has recurrent vesicles which become turbid; they do not extend, but they dry up and in a week or two the scabs fall off. The findings have been exactly similar to those described by Dr. Simpson. I have had impetigo herpetiformis in mind, and dermatitis herpetiformis. The boy has tinea amiantacea on the scalp, which quickly clears up with treatment but recurs, and whether this has anything to do with his body condition I do not know.

The President: I would suggest that heavier doses of arsenic should be tried before concluding that he does not respond to it.

Tropical Lichenoid Dermatitis.—P. D. SAMMAN, M.R.C.P. (for S. HARDY KINGSTON, M.B.).

T. G., aged 47, seaman.

History.—According to the patient quite fit until October 11, 1947, when his feet suddenly became swollen and at the same time he developed a rash on his face and limbs which consisted of spots like those now present on his arms, but larger. At about the same time patchy pigmentation appeared and the skin of his back and buttocks became roughened.

He was taken ashore and admitted to a hospital in Santa Domingo, the condition being diagnosed as fish poisoning. In hospital the rash cleared and he was returned to his ship after one month, when the rash recurred almost immediately. He returned to this country in December and reported to the out-patient department at the end of January, complaining of disfigurement.

Mepacrine history.—The patient had never taken mepacrine until July 1947 but from then he took it continually until he was admitted to hospital; at times he was upset by it. On return to his ship he had to take a double dose to make up for the days lost in hospital. He continued to take it until he returned to this country.

Examination shows the yellow staining of mepacrine, especially on the abdomen; there is also a patchy macular pigmentation of the whole body and some areas of depigmentation.

There are a few lichenoid papules on the arms and some papules below the eyes due to follicular plugging. Over the greater part of the back and buttocks there is a severe degree of follicular hyperkeratosis, resembling lichen spinulosus.

The pigmentation and follicular hyperkeratosis are less now than they were a month ago.

Investigation (23.1.48).—W.R. and Kahn negative.

Blood-count: R.B.C. 5.51 million; Hb. 110% (Haldane); C.I. 1.0; W.B.C. 12,400, neutros. 80%, eosinos. 4%, lymphos. 9%, large monos. 7%.

Urine normal.

Dr. W. G. Tillman: Those in the Services saw a number of lichenoid eruptions due to mepacrine. I can remember one with the same form of spiny eruption. I should have thought the papules on the forearms, neck and face and legs were compatible with the diagnosis, though it did occur to me that the pigmentation on the chest and the patches on the upper arm might be tinea versicolor and I would suggest a scraping being examined.

Dr. R. M. B. MacKenna: I thought of pityriasis versicolor when I saw the colour of the skin. I have not seen lesions resembling lichen spinulosus in so-called tropical lichenoid dermatitis but I know they have been described. In this case there are two forms of follicular lesions, viz. spiny and rounded. Possibly the latter are a sign of avitaminosis. It has been suggested in the American literature that in tropical lichenoid dermatitis there may be some fault of the gastric or intestinal mucosæ whereby there is faulty absorption of vitamin A. I would like to ask whether anyone examined the patient's finger nails under a Wood's ray? I have not had the opportunity of making this examination but I believe that in patients who have been taking mepacrine the nails show an unusual type of fluorescence.

Dr. Samman: Scrapings for fungus have not been made. I did, however, examine him under the Wood's light and except for the extraordinarily beautiful colour of his hair from some oil he was using, he showed nothing at all. He has improved during the month we have had him under observation. He has had large doses of vitamin A and a good diet.

POSTSCRIPT.—Scrapings from the pigmented areas have subsequently been examined but no evidence of tinea versicolor or other fungus has been found.

Leprosy Treated with Sulphetrone in 1943.—A. H. HARKNESS, M.R.C.S., L.R.C.P., and G. BROWNLEE, Ph.D.

Man, now aged 53.

Lived for seven years in British Guiana and during 1927 was employed for some months in the erection of an electric light plant and a cinema in a leper colony. The patient, whilst travelling by air in 1934, became aware of areas of anæsthesia on the extensor aspect of the left thumb and forearm but a diagnosis of leprosy was not made until a year later in Jerusalem. Previous treatment consisted of weekly injections of iodized moogrol.

When first seen by us there were multiple nodules, a trophic ulcer on the right foot and nervous involvement of the chest and upper and lower limbs. An excised papule showed a typical histological picture with large numbers of *My. lepræ*, and nasal swabs were also positive. Treatment with sulphetrone by the mouth commenced in October 1942. A dosage of 1.5 grammes for five days was gradually increased to 6.0 grammes daily, and for a short period 7.0 grammes daily were taken; fluids were restricted to 3 pints (1.7 litres) daily. The drug was administered continuously over a period of fifteen months. Adjuvant treatment consisted of ferrous sulphate 3 grains twice daily. There were no toxic manifestations. Hæmoglobin, averaging 70%, fell on one occasion to 60% and blood levels of sulphetrone varied between 2 and 3 mg. per 100 ml.

All nodules were absorbed during treatment and no fresh ones have appeared. Nasal swabs became negative after twelve months' treatment and have remained so.

There has been no extension of nervous involvement and the same areas show anæsthesia but tactile sensation in the fingers has improved as shown by the fact that the patient is now able to count and distinguish coins in his pocket. The general health of the patient has improved considerably and he has put on weight.

Several reports from Nigeria and India have recently appeared concerning the good results obtained with sulphetrone in the treatment of leprosy and we thought it would be interesting to show the first case treated with this preparation.

Dr. G. Brownlee: The interest in drugs of the "sulphetrone" type arose from the demonstration of the potent antibacterial activity of diaminodiphenylsulphone described by Buttler and others in 1937. It was the chemotherapeutic efficiency of the drug which stimulated our chemical colleagues to prepare a series of derivatives which would retain the activity but without the toxicity of the parent compound. Between 1936 and 1940, a series of Schiff's bases had been studied and appeared to give a favourable lead. Two derivatives, piperonylidene- and cinnamylidene- diaminodiphenylsulphone, justified a complete pharmacological study. They proved satisfactory from the antibacterial aspect, particularly against acid-fast organisms, but had to be rejected because of their tendency to produce peripheral neuritis. However, the progress made justified the testing of soluble derivatives which might prove to be free from these defects, and my attention was directed to a soluble derivative first prepared in 1936. This was sulphetrone. Its chemical name is tetrasodium

4: 4'-bis (γ -phenylpropylamino)-diphenylsulphone- α : γ : α' : γ' -tetrasulphonate. It is insoluble in alcohol and other organic solvents but is exceedingly soluble in cold water. Brownlee, Green and Woodbine (1948) described its structure, chemical and physical properties, its pharmacology, experimental therapy and possible clinical uses. This was followed by a description (Brownlee and Kennedy, 1948a) of the suppressive effect of sulphetrone on progressive experimental tuberculosis in groups of guinea-pigs. The drug was found to be bacteriostatic in action. In a second study (Brownlee and Kennedy, 1948b) showed sulphetrone to be more efficient than promin in protecting the laboratory animal against experimental tuberculosis and to be synergic with streptomycin. The combined effects were impressive enough to justify a clinical trial, unfortunately restricted to a limited series (Madigan, Swift, Brownlee and Payling-Wright, 1947). Simultaneously the drug was under test against leprosy, the case shown to-day being one of the first. Others have been described by Muir (1948) and by Wharton (1947).

The drug has four sulphonated side chains and is a large molecule. Unlike other diaminodiphenylsulphone derivatives, sulphetrone is not hydrolysed in the body; it is therefore well tolerated and may be exhibited continuously for long periods. This patient has had continuous drug therapy for fifteen months. However, sulphetrone has well-defined hematotoxic actions of an interesting kind. It is capable of reacting with alimentary iron to give a non-absorbable complex and thus inducing a hypochromic anemia. This may be prevented by the administration of adequate amounts of oral iron. Sulphetrone is incompletely absorbed and thus is capable of modifying the micro-flora of the gut. Since biosynthesis is frequently a limiting factor in the supply of essential components of the B vitamin complex, alteration of the flora may cause deficiency states. One is an anemia of nutritional origin. It was discovered that simultaneous administration of fresh yeast prevented its development. A third anemia, a hemolytic anemia associated with crenation of red cells and increased fragility, is caused by drugs of this kind. It is continuous during the period of exhibition and may result in a fall of circulating haemoglobin corresponding to 60% Haldane in extreme cases.

The chemotherapy of acid-fast organisms should logically employ the highest blood concentrations that are tolerated by the patient, with the possible advantage of shortening the time of recovery and avoiding the development of resistant strains. Both Muir (1948) and Wharton (1947) gave smaller doses than those employed by Harkness. However, at the blood concentrations employed by all three workers, the problems of toxicity I have mentioned become minute.

An interesting clinical point is that Harkness, treating an intelligent patient, was able to leave the details of drug dosage to his patient.

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Dr. J. A. O'Connor: Some speakers mentioned the activity of sulphetrone against the tubercle bacillus. Is it not possible that a simpler compound such as para-amino-salicylic acid, which is now being tested in tuberculosis, would be equally efficacious in cases of leprosy? The molecule is much simpler, and the drug appears to be tolerated in very considerable doses, even as high as 10 to 15 grammes a day by mouth. Blood concentrations can be got up to 10 or 15 mg. per 100 ml. of blood. Para-amino-salicylic acid is excreted very rapidly without producing toxic side-effects and I wonder whether Dr. Harkness or Dr. Brownlee has considered the possibility of using some substance such as this in the treatment of leprosy.

Dr. Brownlee: We are only at the beginning of the chemotherapy of this difficult group of organisms and we have all been interested in the report on the chemotherapeutic action of para-amino-salicylic acid. Of course, its application should be encouraged. It should prove a cheaper drug than sulphetrone to make and, should clinical trial prove it to be effective against *Mycobacterium tuberculosis*, it is likely to prove more effective against *My. leprae*.

Dr. O'Connor: This particular drug appears to be unusually potent. I saw some microscopic slides recently from a case of tuberculous empyema. The preliminary slide showed the pleural fluid to contain many polymorph-leucocytes, and thousands of tubercle bacilli were floating free in the liquid. The patient suffered from a bronchopleural fistula for which she was receiving penicillin; 2 grammes of para-amino-salicylic acid had been injected into the empyema. Examination of the empyema fluid a week later showed that 82% of the tubercle bacilli had been phagocytosed. Whether this was due to the combination of the drug with penicillin I do not know, but the fact remains that there was this marked degree of phagocytosis and perhaps the same thing could occur in other diseases due to acid-fast bacilli.

The following case was also shown :

Erythema Elevatum Diutinum.—Dr. E. LIPMAN COHEN.

(This case may be published later in the *British Journal of Dermatology*.)

Section of Obstetrics and Gynæcology

President—A. J. McNAIR, F.R.C.S., F.R.C.O.G.

[January 16, 1948]

DISCUSSION ON THE MANAGEMENT OF UTERINE INERTIA IN THE FIRST STAGE OF LABOUR

Mr. D. M. Stern: Uterine inertia is a condition occurring in the course of labour when the contractions are demonstrably weaker, less frequent or shorter than normal. During the first stage of labour the effect of the contractions is to dilate the cervix; therefore when inertia is present this dilatation proceeds more slowly, leading to prolongation of labour. Arbitrarily, it may be assumed that when labour lasts more than twenty-four hours some degree of inertia is present. There is some difficulty in assessing the length of labour. Generally it is measured from the onset of painful uterine contractions, a subjective symptom not always coincident with the beginning of labour which, theoretically, should be measured from the start of the dilatation of the cervix.

Divergent opinions are found in the textbooks as to the cause of inertia, its treatment and results. Therefore, these remarks are based on the experience of a series of some 5,000 cases.

The causes may be summarized: (a) Badly fitting presenting part; malpresentation and deformity of the foetus; abnormalities of the birth canal, including placenta prævia; prematurity, hydramnios and twins; small head in a large lower segment. Over-distension of the uterus is not a factor here. (b) Psychological causes—fear and ignorance. (c) Congenital causes—hypoplasia of the genital organs. (d) Hormonal. (e) Age, especially in primiparæ. (f) Multiparity—not seen much to-day in this country. (g) Drugs and poisons, especially early in labour. (h) Accidental antepartum hæmorrhage. (i) Full bladder and bowel. *Alleged causes:* (a) General debility and disease—no evidence of this in the present series. (b) Early rupture of the membranes tends to increase rather than reduce uterine contractions. When associated with inertia the latter is due to a badly fitting presenting part. (c) Fibroids—only when associated with age, hormonal or congenital causes. (d) So-called rigid cervix—probably the result of hypertonic type of inertia.

Treatment.—(a) Prophylactic; correction of abnormal presentation. Removal of fear and ignorance. Attention to bladder and bowels. (b) Active treatment—not practised in the present series. (c) Passive treatment—rest, food, drink, sedatives (chloral, pethidine, morphia, pentothal); attention to bladder. Present condition of the patient should be treated and the length of labour ignored.

	Primiparæ			Forceps		Total foetal mortality		Maternal mortality
Total deliveries	23,051	13,528	58.7%	1,552	6.7%	1,498	6.5%	61
No. of labours								
over 24 hours	4,854	3,692	76.1%	785	16.2%	312	6.4%	11
24-48.. ..	3,625	2,623	72.4%	498	13.7%	204	5.6%	6
48-72.. ..	851	725	85.2%	171	20.1%	50	5.9%	2
72-96.. ..	252	230	91.3%	74	29.4%	32	12.7%	3
96-120.. ..	79	73	92.4%	26	32.9%	21	26.6%	0
120 and over..	47	41	87.2%	16	34.0%	5	10.6%	0

Professor H. J. Drew Smythe: For the management of inertia in the first stage of labour, it is necessary first to determine the type of inertia present.

There are three main types of primary inertia. The first is characterized by ineffectual contractions from the commencement of labour. Pains are poor, and may continue so for several days. The presenting part is well adjusted to the lower segment, and the membranes do not rupture early. Contraction and retraction are feeble. This is true primary inertia.

The second is the "colicky" uterus described by Miles Phillips. The patient has strong painful contractions from the commencement of labour. Nevertheless the cervix is slow to dilate, the membranes rupture early and the onset of foetal and maternal distress is common. This type of inertia is often associated with posterior positions of the vertex, and with the android pelvis. It is due to loss of polarity of the uterus.

The third type is that which is associated with fear. From an early stage of labour, the patient becomes hysterical, and calls out for immediate delivery. There is no relaxation by the patient between pains, and during them she uses every voluntary muscle against the uterine forces. There is inhibition of cervical dilatation by the higher centres.

In treatment of the first type, the prolonged use of sedatives only worsens the condition. It is essential that these patients should remain active during the day, and a sedative be given

only at night, to ensure sleep. Usually the cervix will dilate gradually, but it may take several days; there is no danger as long as the membranes remain intact. If the membranes do rupture, then our anxiety is increased, and intervention may be necessary. Once the cervix is fully dilated, forceps delivery is indicated. Special care must be taken during the third stage, as again inertia may be experienced. The placenta should not be allowed to remain *in utero* for more than two hours, as definite shock is associated with its retention beyond this limit.

In the second type, sedatives are definitely indicated throughout the first stage. The usual mixture of pot. brom., chloral and tr. opii at three-hourly intervals is helpful in the early stages. Nembutal and other barbiturates can be used instead at this stage. When the cervix has reached quarter dilatation, pethidine in combination with chloral gives good results. With the onset of foetal or maternal distress, further management depends on the cervical dilatation. If the cervix is half-dilated, then manual dilatation is usually successful. If dilatation is not up to half, then incision of the cervix or cesarean section is indicated.

In the third type, if one could detect this from early pregnancy, treatment should commence at once by lessons in relaxation, and by gaining the patient's confidence. It is most important in all cases, and especially so in this third type, that the patient should be, during the antenatal period, in the care of the obstetrician who is to attend her at the confinement. This type may, sometimes, be foreseen, or may come as a complete surprise when labour commences.

Treatment of these cases is by explanation of what is occurring, and the necessity of the process, and by the giving of sedatives. Morphia is indicated at night, twilight sleep is an alternative. On full dilatation, early application of forceps is often indicated owing to the importunity of patient or relatives.

Secondary uterine inertia may occur during the first stage, but is almost certain to be due to disproportion, and operative interference is necessary.

Mr. J. V. O'Sullivan: Inertia means the prolongation of labour over thirty hours. A cardinal sign of inertia is slow dilatation of the cervix which in bad cases remains at 2-3 fingers for three or more days. Dilatation of the colon is also well marked in severe cases.

Treatment.—In all cases of inertia a cause should be sought and disproportion excluded. If disproportion is present the treatment is often surgical, but apart from these cases medical treatment will succeed in the great majority of patients. All cases of inertia should be treated as test labours, and given plenty of glucose and carbohydrates to prevent acidosis, and tests should be made regularly for acetone in the urine.

Only mild sedatives such as pot. brom. 20 grains, and chloral hydrate 30 grains, should be given during the first stages, but later pethidine 100 mg. should be added. The administration of sedatives should be avoided for as long as possible. Morphia should never be given as a routine. It is essential, however, in cases due to fear, tonic uterine contraction, or for cases with ruptured membranes and severe constant backache.

Patients suffering from inertia should be given all possible encouragement and attention, a treatment described by Smellie as "beguiling the patient".

Uterine stimulants.—An ordinary oil bath and enema are useful in many cases, but should not be repeated. Oestroform, up to 100,000 units, is an aid in some cases associated with prematurity or postmaturity. Pitocin, 1 to 2 units half-hourly, may be given when the membranes are intact and there is no foetal distress or disproportion.

Sepsis.—Sepsis should be prevented or controlled by giving sulphonamides and penicillin as a routine to all cases of inertia.

After seventy-two hours the danger of foetal and maternal distress, if not already present, is imminent and the risk of cesarean section increases. Hence on the third day a complete obstetric examination should be carried out including an antero-posterior and lateral X-ray examination. A catheter specimen and vaginal swabs should be sent for examination.

Surgical treatment.—(1) Continuous traction is useful occasionally but more especially is it used when the child is dead.

(2) In cases where the cervix is thin, stretched and 2 to 3 fingers dilated, the pains weak and regular, no disproportion expected at the outlet, the head deeply engaged (almost on the perineum), and the mother or baby showing signs of distress, I recommend *cutting the cervix* at 9 and 3 o'clock for half an inch each side and then gently pushing the cervix up, especially in front. No anæsthetic is necessary, or at most only gas and air. Some of these patients deliver themselves spontaneously in six to eight hours, others require a low forceps.

(3) Where there is foetal or maternal distress which necessitates immediate delivery, I recommend a large medio-lateral *perineotomy* then, under direct vision or under touch, I again cut the cervix, if 3 fingers dilated, at 3 and 9 o'clock, but if only 2 fingers at 12, 8 and

4 o'clock. In each case the incision should be taken to the lateral fornix taking special care not to cut the vaginal wall as the fornix is approached. This part of the operation is sometimes difficult. I then apply forceps and deliver, first doing manual rotation where necessary.

(4) Cæsarean section has only very limited use in the treatment of inertia. It is obviously necessary for all cases of disproportion with early maternal or foetal distress.

I usually perform a lower segment transverse incision in the uterus except in cases of contraction ring, general tonic contraction and certain cases where the foetus is very large and the head fixed firmly in the brim with little liquor in the uterus, when I do a so-called lower segment vertical incision. There is no doubt in my mind that cutting of the cervix in suitable cases in young women is better than cæsarean section.

In some cases where the child is large and post-mature and the widest diameter not through the brim, the cervix thick and not more than 2 to 3 fingers dilated, I recommend lower segment cæsarean section even where the child is dead, because I believe it is safer and better for the mother. I believe G. F. Gibberd agrees with this method of treatment in suitable cases.

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Professor W. C. W. Nixon: Until recently it was difficult, if not impossible, to assess the activity of the uterine muscle at a three dimensional level—centimetres, grammes, seconds. This is now possible with Lorand's tocograph (1947). It is now possible even for the un-initiated to measure uterine action with accuracy especially when Lorand's more recent instrument, the tocometer, is used. Professor Douglas Murphy (1947) obtained his results with Lorand's earlier model and not with the improved tocograph.

Tables I, II, III, have been prepared by Mr. Ian Fraser, Obstetric Registrar at University College Hospital. The figures represent the years 1946 and 1947 together.

TABLE I.—PROLONGED FIRST STAGE OF LABOUR
Incidence at University College Hospital in the Years 1946-1947

Total number of deliveries	2,385
Cases with prolonged first stage of labour (more than 48 hours)	182 (7·6%)
Average length of first stage in these cases (longest first stage 171 hours)	69·4 hours

TABLE II.—PROLONGED FIRST STAGE OF LABOUR
Course of Labour in 182 Cases. Compared with all Deliveries over Years 1938-1947

	Prolonged first stage of labour 1946-1947		All deliveries 1938-1947
Number of infants delivered	186	9,770
Spontaneous delivery	135	89·8%
Forceps	33	6·5%
Cæsarean section	18	3·8%
Incidence of cæsarean section for uterine inertia	{ 1946 5% 1947 13%		

TABLE III.—FOETAL MORTALITY IN PROLONGED FIRST STAGE OF LABOUR
Comparison of Mortality in 182 Cases of Prolonged First Stage in 1946-1947, with Mortality of all Infants Delivered 1938-1947

	Prolonged first stage of labour 1946-1947		All deliveries 1938-1947
Infants delivered	186	9,770
Total infant mortality	8*	5·9%
Stillbirths	7*	3·8%
Neonatal deaths	1	2·1%
(3 of above infants died late in first stage)			
Where membranes ruptured over 24 hours prior to delivery—			
Cases	45	
Infant mortality	3*	6·7%

*Includes one infant with gross congenital abnormality.

Prophylactic treatment.—Uterine inertia has its highest incidence among primipara. Encouragement, sympathy, explanation and the administration of the proper sedative at MAY—OBSTET. 2

the right time can do much to allay fear and remove the inhibiting effect this has upon the dilatation of the cervix. Active movements in the early part of the first stage should be encouraged. Fluid balance and the nutrition of the parturient woman need to be carefully controlled.

Treatment of established uterine inertia.—For long it has been the practice to administer sedatives. In many instances after a period of mental rest the woman has proceeded to deliver herself normally.

Pituitary extract.—The haphazard use of this powerful drug is rightly condemned, but there does seem to be a place for it in selected cases of uterine inertia. By the use of Lorand's tocograph it is possible to determine which case would benefit from such treatment. In the presence of disproportion, malpresentation, excessive parity, the drug is dangerous. Again if the tracing shows the uterus to be in a state of hypertonic inertia an oxytocic drug should never be given. It is when the tracing shows hypotonic inertia (low resting tone, infrequent contractions with a low amplitude) that the case is an ideal one for this therapy. The effect of the first injection (pitocin 1 unit) is seen within a few minutes and the time when the next injection should be given will be clearly indicated. Lorand's classification of inertia into hypotonic, normotonic, hypertonic is of practical value. The tocograph has revealed that there is a type of inertia associated with hypertonus of the uterus that usually has to be terminated by operative delivery.

The effect of pitocin (2 units) when given in the first stage of labour will be seen from the following tracings:

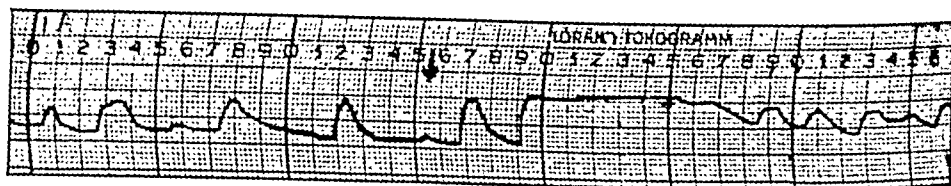


FIG. 1A.—39 years, para-0, normotonic inertia. Pitocin (2 units). Spasm followed by normal rhythm, seventeen hours after labour onset and sixteen hours before delivery.

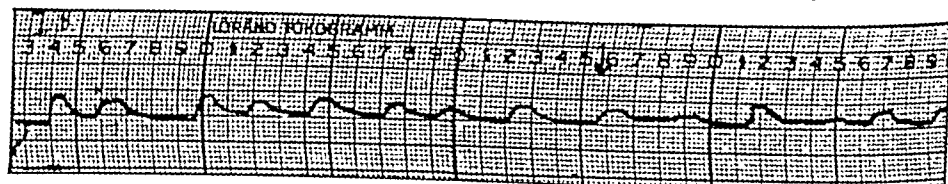


FIG. 1B (Same patient).—Normotonic inertia. Pitocin (1 unit in 1 c.c. sterile water). No effect.

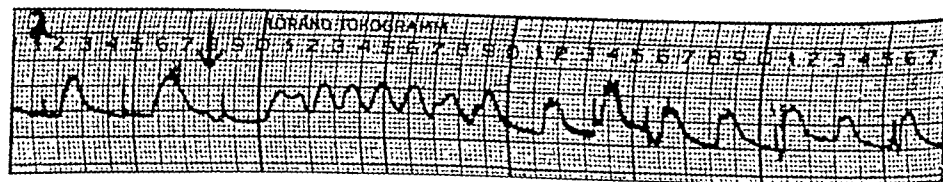


FIG. 2.—30 years, para-0. Pitocin (2 units) eighteen hours after labour onset, twenty hours before delivery. Resting tone and contraction frequency increased.

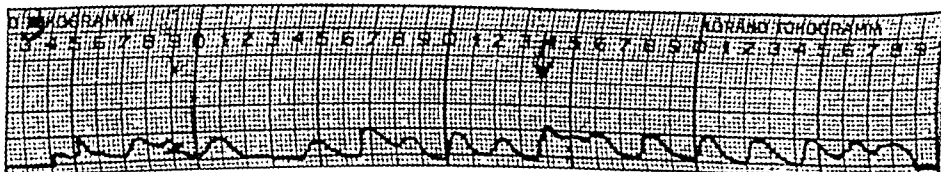


FIG. 3.—30 years, para-0. Hypotonic uterus. Pitocin (2 units) injected twice, twenty-one hours after labour onset, delivery three hours after last injection.

Eastman (1947) gives pituitary extract (initial dose $\frac{1}{2}$ minim and repeated at half-hourly intervals) only after labour has been stationary for eighteen to twenty-four hours with the os dilated 3 to 4 cm. Disproportion and multiparity are contra-indications.

Operative interference.—This can be considered under three headings: (1) Rupture of the membranes; (2) Dührssen's incisions and instrumental delivery; (3) Cæsarean section.

Every case in which there has been active labour for twenty-four hours should be carefully reviewed with regard to the uterine activity, sedation, and fluid balance. If a vaginal examination has not already been done there is an indication for doing it after this lapse of time.

(1) *Artificial rupture of the membranes.*—Often after rupture of the membranes uterine action, previously sluggish, becomes active and the cervix rapidly dilates. In hypertonic inertia the resting tone of the uterus is abnormally high. This is seen in hydramnios. With rupture of the membranes uterine tone is diminished and uterine contractions thereby increased. The tocograph reveals this conclusively.

(2) *Dührssen's incisions.*—This form of treatment has been abandoned by most obstetricians.

(3) *Cæsarean section.*—At any time delivery may have to be rapidly completed on account of maternal or foetal distress. I believe that the lower-segment operation, transperitoneal or extraperitoneal, together with penicillin and chemotherapy, may be life-saving both for mother and baby. Sheehan (1948) has shown how prolonged labour is the greatest single cause of death from shock.

Colonic distension and atony of the bladder, particularly when this organ, even though empty, becomes drawn up towards the umbilicus, are always ominous. When labour is allowed to be so protracted it is best terminated by cæsarean section for in such a case the cervix is usually incompletely dilated. The triad—uterine inertia, atony of the colon and bladder—points to some common ætiological factor of a paralysing nature.

Much harm has resulted from the teaching that delivery must be at all costs *per vaginam* because the membranes have ruptured. Unnecessary vaginal mutilation predisposing as it does to genital infection has resulted from the adoption of this inflexible attitude in obstetric practice. It is safer to do a cæsarean section than a vaginal operation accompanied by much tissue tearing. Abdominal delivery, when the os is only partly dilated, is accompanied with far less trauma than a vaginal associated with multiple incisions of the cervix, vaginal lacerations and an extensive episiotomy.

As yet I have not regretted terminating certain cases of protracted labour by cæsarean section. I wish that for some of the others I had not shown so much zeal for vaginal delivery.

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Dr. Joyce Morgan said she had hoped to learn more from the discussion about the condition of the tetanic uterus. In her opinion this condition, formerly known as "rigid cervix", was quite different from uterine inertia. Uterine inertia was a condition of weak, infrequent contractions, whereas in the condition of rigid cervix the contractions were strong and frequent.

This is a rare condition, and she had seen only 26 cases out of a consecutive series of 12,000 deliveries. In all these cases the foetal head was on the perineum, and the undilated cervix was pushed out through the vulva, in front of the advancing head. She had treated the first of these cases with cæsarean section, and the last 20 cases by incision of the cervix. Small incisions only were required, the soft lower segment dilating easily after incisions had been made. They healed remarkably well and gave rise to no trouble. There were no maternal deaths in this series.

Two of these cases were admitted to hospital as emergencies after being in labour for five days, and on admission were found to have dead babies, and a contraction ring, though the cervix was not taken up and admitted only one finger.

Dr. Dick Read: Cases of uterine inertia in the first stage of labour may be divided into three groups which are generally accepted as being concerned with labour, but in my opinion the first group is a pre-labour manifestation and should be recognized as such:

Group 1.—Pre-labour contractions without dilatation of the cervix.

Group 2.—Labour contractions with cervical dilatation.

Group 3.—Inertia of mechanical obstruction with arrested dilatation.

Group 1 is important because it is frequently mistaken for labour. A woman from 37 to 40 weeks pregnant feels uterine contractions which soon become severe and painful. The

pain is described as a tight band *round* the lower abdomen and into the flanks. The contractions are often frequent and colicky, and cause considerable distress; vaginal examination reveals a normal cervix—neither open nor taken up. There is probably little or no contraction of longitudinal fibres.

This pre-labour muscular activity is a psychosomatic manifestation, and arises from exaggerated anticipation and desire for labour to begin. It is almost entirely circular fibre spasm from sympathetic nerve impulses. It can be relieved by sedation: morphia $\frac{1}{4}$ grain is sometimes indicated, but the condition must be explained to the woman in simple terms. After a few hours' rest and sedative she is instructed to get up and walk, maintaining good posture and relaxed carriage. Not infrequently she returns home for some days to await the onset of labour with no recurrence of the colic. The contractions of true labour are described as quite different and entirely free from the pain she experienced previously.

Efforts to stimulate these cases are ineffective and often dangerous. During these attacks the infant is not embarrassed, but the pain and distress of the mother may tempt the attendant to interfere, if the condition is not recognized.

Group 2 is also cortico-thalamic in origin to a large extent. Chemical factors and muscular ineffectiveness are probably secondary and not primary phenomena.

In a state of apprehension and fear, the protective, inhibitory impulses to the circular fibres override the motor fibres of the longitudinal uterine axis. Not only resistance to dilatation occurs, but also weakened motor stimuli. Moreover, the sympathetic nerves supply the muscle walls of the arteries to the uterus and, as Langley and Anderson pointed out, when in action, the volume of blood reaching the muscle tissues is markedly diminished.

Thus, the paucity of nutrition, the inhibition of motor impulses and the resistance of the relatively tonic outlet combine to produce a state of inertia. Complete muscular relaxation, patience and self-control enable labour to proceed. Sleep from time to time is essential, and food in the form of light meals should be given freely. With this treatment, labour will usually terminate within seventy-two to eighty hours in a natural delivery. In the first stage of such a labour, stimulation rarely succeeds, and is to be eschewed. The removal of psychological causal factors allows a progressive although slow cervical dilatation, without exhaustion to the mother or danger to the child. The greatest danger is interference, and should not be resorted to unless clearly indicated by the condition of either the mother or her infant.

Group 3 is an obstetric emergency, and early diagnosis of obstruction to the presenting part is the key to success. The treatment in the first stage is one of three methods: (a) Cæsarean section. (b) Manual or operative dilatation of the cervix and forceps extraction if necessary. (c) To wait for full dilatation and allow delivery or deliver vaginally.

This type of inertia may be dangerous to both mother and child. The infant may suffer from prolonged, frustrated pressure. The mother may become rapidly exhausted and shocked. When diagnosed, the course indicated should be adopted without delay, in spite of apparently weak contractions.

Dr. R. G. Maliphant: Classical uterine inertia is not a common condition and rarely causes practical difficulties. The serious obstetric problem is the irritable uterus commonly seen in association with posterior position of the occiput and in cases of minor disproportion. Uterine action, though vigorous, is inco-ordinate and ineffective, and labour comes to a standstill in the course of the first stage. In my view, cæsarean section has a definite but small place in the management of this condition, and should be reserved for cases in which the cervix has not been well 'taken up'. Usually the cervix is thinned out and manual dilatation followed by forceps extraction is the method of choice. Subsequent confinements in these women take a fairly normal course.

Mr. John Howkins: In the anatomical approach to the problem of the innervation of the uterus we find that the pain centres for the uterus in the cord are situated somewhere between D.11 and D.12, and can be blocked by a local or caudal anæsthetic going to this level and not higher; if the caudal is taken higher, as has happened in one of my cases, above D.6, the centres in the cord which subserve uterine contraction are inhibited, and a strong labour can be converted into a case of primary inertia. A better understanding of the anatomy of the nerve control of uterine contractions in labour might enable one to inhibit spasm, rigidity and lack of polarity in the cervix, without upsetting the power of the detrusor muscle of the uterus.

[February 20, 1948]

DISCUSSION ON THE TREATMENT OF SEPTIC ABORTION

Dr. A. Melvin Ramsay: The London County Council Puerperal Sepsis Unit at the North Western Hospital, Hampstead, with which I have been associated since 1937, has been the only Unit of its kind in London since the Isolation Block at Queen Charlotte's closed in 1939. We have therefore had a unique opportunity to study the problems of post-partum and post-abortion infections. The relative incidence of the latter has risen steadily; whereas in 1932 only 16% of our cases were post-abortion, in 1945 the number had risen to 55.9%.

We deal entirely with infected cases and our treatment has therefore tended to be along conservative lines since we feel that intra-uterine manipulation may facilitate spread of infection; indeed, we believe that, with inexperienced or over-enthusiastic operators, it can prove disastrous. No doubt with the advent of penicillin that danger has been considerably modified but that is all the more reason why we should face clearly the lessons that accrue from past experience under less favourable conditions and I certainly very strongly deprecate the attitude that penicillin therapy permits of laxity either in bacteriological investigation or in the application of sound principles of treatment (Kenny, 1945).

The general hospitals deal with the uninfected incomplete abortion daily, and in skilled hands the removal of retained products is a perfectly safe procedure nor can there be any objection to it as a principle of treatment. It is in the case of the infected incomplete abortion that a conservative attitude is defensible even in this penicillin era.

The routine at the North Western Hospital has been to delay vaginal investigation for some hours after admission; careful observation of the general condition and pulse-rate will indicate the presence of an early peritonitis or septicæmia and if either of these is suspected, treatment is at once instituted. Otherwise the patient is given a good night's rest and is then examined in the lithotomy position the following morning. When retained products are present in the cervical canal they are grasped firmly with an ovum forceps and removed. An examining finger may then be passed into the uterus but intra-uterine manipulation is avoided; we are firmly convinced that it is this latter procedure that may prove dangerous in that it breaks down the natural lymphocytic barrier and so tends to cause spread of the infection. If hæmorrhage demands it, however, removal is carried out under intravenous pentothal anaesthesia.

In an analysis of our results for the ten-year period 1937-46, 1,430 cases of post-abortion pyrexia were dealt with; 1,217 of these had infection localized to the uterus and ranged from mild to severe types. In only 97 (8.0%) was removal of retained products under general anaesthesia performed and of these 31 had been done before admission to the Unit. In other words, 92% of these cases recovered without intra-uterine manipulation. We aimed at establishing adequate drainage with Fowler's position and intra-uterine glycerin in certain cases. We found that pyrexia subsided much more rapidly than in the post-partum cases. The average stay in hospital was ten to twelve days. During that time portions of placenta would frequently be passed without hæmorrhage and with no general disturbance; all cases were re-examined before discharge and no patient was allowed to go unless the os was closed and the uterus well involuted. Only in 3 of the 66 cases in which we removed retained products could I find any evidence that we had done so on account of persistence of pyrexia and with subsidence of the same after removal.

In the remaining 213 cases invasive complications of various kinds were present and these may be analysed as follows:

Type of invasive complication	No. of cases	No. of cases with removal under gen. an.	No. of fatal cases	No. of fatal cases with removal under gen. an.
Pelvic infections	130	9	6	1
General peritonitis	13	3	8	2
Septicæmia	54	15	30	11
Metastatic and other infections	16	4	3	1
Total	213	31 (14.5%)	47	15 (31.9%)

Of the 31 cases which had removal under general anaesthesia 22 were done before admission to the Unit; of the 15 in the fatal group 12 were done before admission.

The incidence of removal under general anaesthesia (14.5%) is almost twice that in the uncomplicated group while the rate in the fatal cases (31.9%) is nearly four times as great. One is struck also by the high rate of removal associated with the more severe invasive complications, e.g. 27.8% of the septicæmia cases had removal under general anaesthesia but only 6.9% of the more benign pelvic infections. Among the fatal septicæmia cases the rate of removal was still higher, namely 36.7%. More important still is the fact that at least 19 of the 31 cases had removal performed before the infection became generalized.

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Thus, the paucity of nutrition, the inhibition of motor impulses and the resistance of the relatively tonic outlet combine to produce a state of inertia. Complete muscular relaxation, patience and self-control enable labour to proceed. Sleep from time to time is essential, and food in the form of light meals should be given freely. With this treatment, labour will usually terminate within seventy-two to eighty hours in a natural delivery. In the first stage of such a labour, stimulation rarely succeeds, and is to be eschewed. The removal of psychical causal factors allows a progressive although slow cervical dilatation, without exhaustion to the mother or danger to the child. The greatest danger is interference, and should not be resorted to unless clearly indicated by the condition of either the mother or her infant.

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TABLE I

Year	No. of cases	No. extracted	Septic	% Septic	Total deaths
1942	396	160	36	22.5	2
1943	443	443	86	19.4	1
1944	388	153	20	13	2
1945	357	128	17	13.3	3
1946	362	125	10	8	1
1947	371	371	70	18.9	1
Total	2,317	1,380	239	17.3	10

It will be noted that the approximate percentage of septic cases varied from 8 to 22.5%. The total percentage of septic cases among those analysed was 17.3%. The total number of deaths for the period was 10. That is a mortality of 0.43% for the total number of cases, 2,317.

Treatment.—First, immediate surgical intervention, and secondly, a course of chemotherapy followed by intervention. In the cases under review excessive hæmorrhage was considered the only reason for immediate operative interference in the presence of pyrexia. In these cases a digital curettage followed by a flushing douche of dettol was performed. Packing was not carried out routinely but only in cases where the placental débris proved abnormally adherent and separation of this caused a free hæmorrhage which was not controlled by uterine contractions. In all other cases with pyrexia associated with slight bleeding the conservative method was adopted. Chemotherapy was given and when the temperature had been normal for forty-eight hours evacuation of the uterus was performed. Here again a uterine pack was seldom used except to control bleeding. The incidence of packing can be seen in Table II. In the whole series packing was found necessary on eight occasions. In the grossly infected cases where the infection had spread to the tubes or pelvic peritoneum intervention was only undertaken in those cases which continued to bleed. Conservative treatment was adopted in the cases of salpingitis, parametritis or pelvic peritonitis unless a localized pelvic abscess formed and then a posterior colpotomy was done. Pelvic abscess occurred in six cases in the whole series. Spontaneous drainage of the abscess occurred in two cases. In one the abscess had burst spontaneously into the rectum before admission, in the second a foreign body had been pushed through the posterior fornix and the abscess was draining through this opening.

Transfusions.—Only in 25 cases was blood transfusion considered necessary. Hæmorrhage was found not to be a marked feature in septic cases.

Table II gives an analysis of the cases with the method adopted and the complications of the cases.

TABLE II

Year	Septic cases	D & C	Pack	D & C not done	Trans- and para-fusion	Salpingitis and parametritis	Peri-tonitis	Pelvic abscess	Septi-cæmia	Deaths
1942 ..	36	29	0	7	2	1	1	0	2	2
1943 ..	86	71	2	13	7	3	2	3	4	1
1944 ..	20	16	0	4	3	4	1	0	0	2
1945 ..	17	11	1	5	3	0	0	0	0	3
1946 ..	10	8	1	1	4	1	0	1	1	1
1947 ..	70	49	4	17	6	8	2	2	0	1
Total	239	184	8	47	25	17	6	6	7	10

Bacteriology.—Cervical swabs were taken on admission and blood cultures when generalized infection was suspected. The commonest causal organisms were *Bacillus coli* and *Staphylococcus albus*. There were a few cases of infection by hæmolytic streptococci, anaerobic streptococci and *Cl. welchii*.

Chemotherapy.—In the earlier years the sulphonamides were given; latterly penicillin alone or penicillin in conjunction with sulphonamides in grossly infected cases. In gas gangrene infections anti-gas gangrene serum was given.

Deaths.—The causes of the 10 deaths were then fully reviewed by the author, and summarized as follows: Gas gangrene was the cause of death in 4 cases; septicæmia in 2; lacerated uterus (criminal abortion) in 1; acute nephritis 1; bronchopneumonia and septic nephritis 1; and shock 1 (due to insertion of corrosive fluid into the pregnant uterus).

Summary.—239 cases of septic abortion have been considered. These are unselected cases from a total of 2,317 abortions occurring over a period of six years. There were 10

8 of the pelvic infections, 7 of the septicæmia cases and all 4 of the metastatic group had removal carried out before there was any evidence of spread of infection. On the other hand, one of the pelvic group, all 3 of the cases of generalized peritonitis and 4 cases of septicæmia had the removal done after the infection had spread. In the remaining 4 septicæmia cases it was difficult to decide from the records whether spread of infection preceded or followed the removal as the two events appeared to coincide closely.

As the septicæmia group showed the highest percentage of removal under general anæsthesia a fuller analysis was made and this resulted as follows:

Type of organism	No. of cases	No. of cases with removal under gen. an.	No. of fatal cases	No. of fatal cases with removal under gen. an.
<i>Staphylococcus aureus</i>	24	5	10	2
Anaerobic streptococcus	14	7	11	7
<i>Clostridium welchii</i>	8	1	3	—
Hæmolytic streptococcus (Group A3, Group B4, Group G1) ..	8	2	6	2
Total	54	15 (27.8%)	30	11 (36.7%)

This analysis shows that removal of retained products is predominantly associated with the most lethal of the post-abortion group of organisms, namely the anaerobic streptococcus. I may say that in post-partum infections with the same organism there is a very clear connexion with the intra-uterine manipulation entailed in manual removal of adherent placenta.

We have post-mortem records of 46 of the 47 deaths which occurred in this series. In the 32 cases in which no removal had taken place, the records show that no placenta remained in the uterine cavity in 26 and of the remainder only small fragments were found in 5; a spongy mass of what was probably altered placenta was found in the sixth. Retained products which are left in situ are therefore either passed naturally or may to some extent be liquefied and pass in the lochia.

Admittedly the position has been altered by the advent of penicillin since most of the organisms that are responsible for post-abortion infections yield to it whereas sulphonamide therapy in established infections was consistently disappointing. But penicillin has provided us with a powerful reinforcement to Nature's restorative processes and should be used as such and not as an excuse for routine interference. I am certain that caution is needed in dealing with a case of severe spreading infection especially if peritonitis is present. A multipara aged 34 was admitted with acute toxæmia following abortion; well-marked icterus and a very low pulse pressure signified a *welchii* septicæmia which was subsequently confirmed bacteriologically. In addition she had an extensive pelvic peritonitis. I was urged to remove retained products in order to "eliminate the focus of infection". I declined to do so and advised the institution of combined penicillin and sulphonamide therapy first. The following morning I was able to remove a large mass of foul placenta without an anæsthetic. But if that had not been practicable I should have refrained from the administration of a general anæsthetic to a patient so toxic, with a blood-pressure of 80/60 and with such extensive peritonitis.

I trust I have been able to show from this investigation that in cases of infected abortion: (1) The most important principle in treatment is the control of the infection; (2) there is no necessity to carry out a routine removal of retained products under general anæsthesia in every case; (3) removal of retained products under general anæsthesia seldom exercises any beneficial and may indeed exert an adverse effect on the course of the infection.

REFERENCE

KENNY, M. (1945) *J. Obstet. Gynaec.*, 52, 4.

Dr. I. R. Bishop: It seems to me that the crux of the problem in septic abortion is the method of treatment. With this in view I have attempted to carry out an analysis of over two thousand cases of abortion admitted to St. James' Hospital, Balham, during the years 1942-47 inclusive.

The criteria for the diagnosis of septic abortion were similar to those adopted by Stallworthy, namely that an abortion was considered septic when associated with pyrexia for which no other cause was found, with offensive or purulent discharge, or with evidence of pelvic infection. Cases with pyrexia only during the process of abortion were not considered septic. Unfortunately during the war years owing to a shortage of medical and clerical staff the system of filing of the notes has made it impossible to analyse all cases but I have succeeded in extracting over thirteen hundred unselected cases, the distribution of which is shown in Table I.

Dilatation of the os was avoided if possible, retained products were loosened with the gloved finger and removed with ring forceps. Curettage, intra-uterine glycerin, uterine packing, oxytocic drugs and douching were all avoided, and hæmorrhage was controlled by bimanual compression. Dilatation of the os, however, had not been proved to be harmful, and figures quoted showed that no different results were obtained in cases where dilatation of the os was done and where it was avoided.

Types II and III cases were treated conservatively with sulphonamides and penicillin, and appropriate sensitivity and blood concentration tests were done if the response was inadequate. Sulphathiazole up to 80 grammes, and penicillin up to 10,000,000 units, have been found necessary in some cases. A pointing abscess was opened and drained, but posterior colpotomy was only necessary on one occasion. Pelvic masses rising into the abdomen were carefully outlined with a skin pencil, and if they continued to enlarge were also opened. Once the acute phase was over local heat was applied in the form of intrapelvic diathermy, and was continued if necessary for two to three months.

Average length of stay in hospital was 19.9 days, compared with 9.7 days in the case of non-infected abortions.

There was one death from septicæmia, the patient dying shortly after admission to hospital.

An analysis of the associated organisms showed that *B. coli* was most frequently encountered, being present in 30% of cases. Hæmolytic streptococci were only found on 8 occasions, and only 2 of these were identified as belonging to Group A. These infections, however, were nearly all severe, and 3 of them spread outside the uterus. *Cl. welchii* infections occurred twice. Anaerobic streptococci had not been isolated, but had probably been the infecting pathogen in some cases in which no growth had been obtained on culture of the vaginal swabs.

The use of propamidine was advocated particularly for anaerobic infections which were sulphonamide and penicillin resistant. This had been given intravenously in doses of 2 mg. per kilogram of body-weight chiefly in cases of thrombosis and embolism following full-time labour, but the good results obtained justified the use of this aromatic diamidine in treating septic abortions if they were not amenable to other forms of therapy.

Mr. John Stallworthy stated that he wished to re-emphasize the principles laid down in the article which had been published from Oxford in the *B.M.J.* of July 19, 1947, over the signatures of Mr. Corston and himself. In fairness to them both, and in view of some of the criticisms which this paper had evoked, he would like to make it clear that it was not claimed by them that the "interventionist attitude" which they supported was in any way original. They had merely published their experience of the treatment of 600 cases by early evacuation and had analysed their results.

The main concept to be emphasized was that the placental site is a wound and should be treated as such. When it is clean no treatment is required; when it is infected then the sepsis requires treatment; when it is bleeding the hæmorrhage must be stopped. He pointed out that the steady moderate hæmorrhage continuing for days or weeks was in the long run often just as dangerous as the more severe acute hæmorrhage of shorter duration. He claimed that he was not speaking with any great practical knowledge of the subject in so far as the total series of incomplete, inevitable and septic abortions handled in his department since its inception nine years ago was only 803. Of the many cases treated in the years before this accurate records were not available, and as impressions were dangerous his comments were confined entirely to the experience gained from this series of 803. The incidence of septic abortion in this series had been approximately 10% and the total number of septic cases analysed relevant to the discussion was only 85. There were, however, certain factors which should be taken into account on the credit side of the picture. They were that all the cases treated were collected in one hospital and its associated annexes. In the event of subsequent complication occurring there was only one hospital to which they could return so that had mishaps occurred as a result of, or in spite of, treatment, these would have been soon discovered. This point was particularly important when one was defending a line of treatment perhaps more radical than that practised by many. Whatever other criticism could be made it would be irrelevant and unfair to suggest that the subsequent progress of cases when discharged from hospital was not known.

In connexion with the treatment of septic abortion it was well to remember that prevention was better than cure. It had often been said that criminal interference was the usual cause of septic abortion. Whether this was so remained to be proved, but it was undoubtedly a common cause and too frequently took its toll not only of the single young woman in distress, but of the mother harassed by a young family, inadequate housing, lack of assistance and lack of money. In such cases a more liberal guidance on contraception as an aid to family planning would do much to help avert the tragedies so often associated with criminal and septic abortion.

deaths in the whole series from which two may be excluded as not due to sepsis, namely the case of shock and the one of abortion occurring spontaneously in a patient suffering from acute nephritis.

8 cases may therefore be said to have died directly as a result of septic abortion out of a total of 2,317 cases of abortion.

The treatment adopted was evacuation of the uterus only after saturation of the blood with sulphonamides or penicillin. It is felt that the risk of generalized spread of the infection as a sequel to intervention is minimized by this procedure and I think the results will support my claim.

Dr. C. W. F. Burnett: A septic abortion is one in which infection enters the body through the genital tract either before or during the process of abortion or during the subsequent puerperium. It is considered evidence of such infection if the temperature is maintained above 99° F. for twenty-four hours during or within two weeks of an abortion, and is not accounted for by any extraneous lesion, or if there are signs of intra-uterine or peri-uterine infection. Cases are considered as severe if the temperature rises above 100·4° F. (38° C.), and are classified into three types: Type I in which infection is limited to the uterus, vagina or perineum; Type II in which infection involves the pelvic cellular tissues, tubes, pelvic peritoneum or veins, and Type III which is associated with generalized peritonitis or septicaemia. At the West Middlesex County Hospital during 1946 and 1947 there have been treated 1,035 cases of abortion, of which 115 were septic, an incidence of 11·1%. 43% were mild cases and 57% severe. 83·5% were of Type I, 13·1% of Type II, and 3·4% of Type III. Criminal interference was acknowledged in 20·8%, but probably accounted for the majority of cases.

Treatment of a Type I septic abortion can be considered under four headings corresponding to the four basic elements in the treatment of infection.

(1) The inhibition of bacterial growth. Our practice is to use antibiotics and chemotherapy after a high vaginal swab, a blood-count, and a catheter specimen of urine have been taken for diagnostic purposes. A blood culture is asked for if the temperature exceeds 102° F. Sulphatriad is used at present (chosen because of the small risk of urinary crystallization) and is given in an initial dose of 6 grammes, followed by 3 grammes four-hourly. A blood sulphonamide concentration of 10 mg% is aimed at, and initial doses are given parenterally if necessary. A daily fluid intake of 6 pints is maintained, and the urine is kept alkaline. Penicillin is given in an initial dose of 100,000 units, followed by 40,000 units four-hourly if the organism is found to be penicillin sensitive.

(2) Prevention of bacterial spread. This is effected by reducing interference to a minimum, and no instrumentation is permitted beyond the removal of any chorionic material that is felt lying in the cervical canal. This is a valuable procedure because it often stops haemorrhage, and spares the patient the necessity of a blood transfusion or immediate transfer to the theatre for evacuation of the uterus. Oxytocic drugs are not given for fear of disseminating infection by muscular contractions of the uterus, and douching is avoided for fear of mechanical spread. Fowler's position is still employed.

(3) Maintenance of the defensive reaction of the body by good diet and nursing. Anæmia is corrected by fersolate or matched rhesus-negative blood transfusions. The temperature sometimes falls dramatically after a transfusion.

(4) Removal of the cause of the infection. This is the most debatable part of the treatment, because surgical evacuation of the uterus is diametrically opposed to the principle of no instrumentation, and may therefore cause spread of infection. If hæmorrhage is severe, the question is answered, and the uterus must be emptied. This was done in 16 cases and no intensification of sepsis or spread beyond the uterus occurred. In the absence of hæmorrhage it is best to wait for the infection to be brought under control before proceeding to evacuation of the uterus. This was done in 39 cases, of which 34 had a mild convalescence after operation and 5 a stormy one, and spread outside the uterus occurred in 2 cases.

However, one should not wait very long for this to occur. If the temperature and pulse do not fall after waiting for twenty-four to thirty-six hours with sulphonamide and penicillin therapy, evacuation should then be performed, provided there is no extra-uterine spread. This was done in 20 cases, of which post-operatively 11 were mild and 9 severe and 3 subsequently spread outside the uterus. These figures appear to justify a policy of waiting and giving the infection an opportunity of being controlled before proceeding to evacuation.

When the infection has been brought under control evacuation can be done after waiting for twenty-four hours; figures quoted showed that results were the same as those achieved by waiting for longer periods up to a week.

Evacuation was found to be necessary in 65% of cases. It was performed under thiopentone anaesthesia, and was preceded by an injection of 250,000 units of penicillin.

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There was, however, another aspect of the subject to which emphasis was given. Just as criminal interference was a cause of many septic abortions so lack of interference, which some day may be regarded as criminal, was responsible for many more. Too often the woman who was admitted with a septic abortion had incompletely aborted spontaneously several days or even several weeks before and had been permitted to continue with retained placental tissue. This was done either because of an unjustifiable optimism that all would be well if left to Nature, or because of a deliberate policy on the part of a medical attendant who had been taught that interference in such cases was dangerous. In over 800 consecutive cases treated at the Radcliffe Infirmary, Oxford, by evacuation there had been only one death and that was in a woman who had aborted incompletely one month previously. There had been daily hæmorrhage subsequently and it was not until one month later when her hæmoglobin was 22% and she was moribund with a terminal *Cl. welchii* septicæmia that she was admitted too late to hospital where she died within twenty-four hours. This case gave further emphasis to the plea for early treatment of incomplete abortion, and it was claimed that by this early treatment many septic abortions would be avoided.

Reference was then made to the technique of therapeutic abortion. It was stated that there could surely be no scope in these days for the two-stage evacuation of the uterus either by tents, bags, plugging or other methods. If it was necessary to terminate a pregnancy on therapeutic grounds, then it should be done as a clean surgical procedure either by dilatation and evacuation in the early stages, or by hysterotomy, vaginal or abdominal, if the uterus was too big for the first manœuvre.

In the treatment of septic abortion once the condition was established it should be remembered that sepsis and anæmia were frequently associated. In the Oxford series blood transfusion was administered in 14% of all abortions treated, but in 25% of the septic group. The two enemies of recovery were hæmorrhage and sepsis. In combating the hæmorrhage two things were essential, to replace any severe blood loss by prompt transfusion and to prevent further hæmorrhage by emptying the uterus. The suggestion made by Dr. Gibbon Fitzgibbon in his paper recently published in the *Journal of Obstetrics and Gynecology of the British Empire* that this order of treatment was incorrect and that the uterus should be emptied first was challenged. It was pointed out that no surgeon would perform a gastrectomy for a bleeding ulcer until he had restored the patient to such a condition as to make operation reasonable and safe. In the same way it seemed that the patient was being submitted to an unnecessary risk if, when she was already exsanguinated, the risk of further blood loss was accepted, when by waiting a very short time her condition could be made safe for operation. These were the principles on which the treatment carried out at Oxford had been based.

Reference was then made to *Cl. welchii* infection and to the terrible clinical picture it presented; the cold clammy cyanosed skin, the almost imperceptible pulse with a blood-pressure which could not be recorded, post-mortem lividity present while the heart was still beating, as if to mock the attempts made to defeat the angel of death, suppression of urine or at the most a few drops of a port-wine colour, but even with the imminence of death the eyes still bright and the mind fully conscious.

It was pointed out that the diabetic patient was rather more liable to infection with gas-forming organisms than the non-diabetic, and reference was made to the work of Kemp who had recorded gas production in the diabetic with both actinomycotic and anaerobic streptococcal infection. A slide was shown illustrating infection of the brain of a foetus *in utero* by gas-forming organisms in a diabetic woman not in labour and herself apparently free from infection. It was pointed out that the only possible source of infection of the foetus was by the maternal blood-stream.

The speaker concluded with a brief summary of the clinical treatment and ultimate recovery of a young woman who within eighteen hours of the induction of a criminal abortion was in an apparently moribund condition with a combined *Cl. welchii* and *B. coli* septicæmia. The uterus was evacuated on the fifth day after admission. The importance of giving eucortin to combat the profound effect of Clostridium toxin on the adrenals was emphasized.

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Section of Comparative Medicine

President—R. E. GLOVER, F.R.C.V.S.

[December 10, 1947]

DISCUSSION ON NUTRITION AND RESISTANCE TO INFECTION

Dr. P. G. H. Gell (*National Institute for Medical Research, Hampstead*): It is usually taken for granted that among human populations mass starvation is an important factor in the genesis of epidemics of infectious disease. Historically, this is by no means easy to demonstrate; so often, famine is only the most painful feature of a situation which includes overcrowding, breakdown of normal sanitary measures, mass movements of population, and general demoralization. All these factors are likely to play a part. However these—except of course the last, the psychological imponderable—do no more than intensify the exposure of the population to infection. Once exposed, the individual may also (as a result of starvation) have a lowered resistance.

Resistance again can be divided up into its various stages. For instance, the non-specific power of the skin to clean itself of pathogens appears to be due, in part at least, to the secretion of fatty acids in the sebum. In cases of malnutrition, at any rate in many of those I saw in Germany, the dryness and flakiness of the skin is extremely striking; one would expect that its self-sterilizing power would have been reduced and in fact German practitioners complained of the excess of superficial skin lesions they were meeting.

Too little is known about these non-specific, surface defences of the human body, especially in generalized pathological conditions such as starvation. Not very much more is known about the effect of starvation on the internal "trigger"-defences, cellular and humoral, that is, those mechanisms which operate before specific immunity has been established—normal antibodies, phagocytosis and so on. However, there is one type of defence one would expect to be affected, namely, the production of antibodies; because this entails the synthesis or at least the adaptation of serum proteins on a fairly large scale, and of course one of the presenting signs of malnutrition is a lowered serum protein.

Indeed the system of priorities which the body follows when it is undernourished is of extreme interest. Everything goes to show that the defence mechanisms are pretty high on the list. One has only to think of the danger of a failure to segregate the bacteria in our own intestines to see why this is so. Nevertheless, a certain amount of experimental work has been done on animals, which goes to show that malnutrition, and especially protein starvation, depress their antibody-response to vaccines and their resistance to infection.

Now protein undernutrition is clearly the best condition in which to investigate depression of antibody-response, because the metabolism of antibody protein is practically bound to be affected.

The situation in Germany in 1946, where the experiments I shall describe were carried out, presented the more usual picture of general caloric undernutrition—a reasonably balanced diet, but not enough of it. This is, however, the characteristic post-war situation, and when Professor R. A. McCance organized a unit, under the aegis of the Medical Research Council, to investigate the physiology of undernutrition, the opportunity was taken to investigate antibody production.

The work was carried out in Wuppertal, a fair-sized industrial township on the edge of the Ruhr, in the summer of 1946. The basic ration at this time was 1,000 calories: in urban districts, severe undernourishment was widespread, though not sufficiently serious to cause clinical symptoms in most of the population. This was the situation in which we set out to investigate antibody production. This is, of course, by no means the only measurable immune mechanism, but it is the simplest to measure accurately.

In order to observe both the primary and the secondary response, it was essential to choose a vaccine to which the subjects could have no pre-formed, latent immunity; and after trials, a somewhat bizarre mixture was chosen, consisting of tobacco mosaic virus, avian red cells, and a saprophytic vibrio. The latter failed to produce demonstrable agglutinins in any of the test or control subjects, and results with it have not been included. Each subject received two injections at an interval of three weeks: the sera were sampled before the first injection and weekly thereafter for five weeks.

The test subjects were divided into two groups: (1) 32 patients selected from those sent up to Barmen Municipal Hospital as cases of malnutrition, and (2) 25 prisoners from the civil gaol at Siegburg, also showing symptoms of undernourishment on clinical examination.

Sixteen normal subjects, mostly British troops, were used as controls.

The results, which are summarized in Table I, were not wholly satisfactory, largely owing to the very low titres attained throughout; this may have been due to the nature of the anti-

TABLE I.—PERCENTAGES OF SERA GIVING AGGLUTINATION AT A DILUTION OF 1:8 OR MORE

Group	versus Fowl Red Cells			versus Tobacco Mosaic Virus		
	Before injection	During three weeks after first injection	During two weeks after second injection	Before injection	During three weeks after first injection	During two weeks after second injection
Siegburg (prisoners)	8.0	60.0	60.0	0.0	52.0	48.0
Barmen (patients)	6.3	37.5	65.5	0.0	53.1	31.3
Normal controls	0.0	81.3	87.5	0.0	93.7	93.7

gens, the time interval of injection, or other conditions. No agglutination was recorded with either antigen at a titre higher than 1/64. The data have been subjected to statistical analysis, and the superiority of control to test groups in all periods, shown to be significant. But is this due to undernourishment?

There is one factor in which the test and control groups differ considerably, namely, the age distribution; the average age of the controls was in the twenties, of the test subjects in the forties. However, the correlation between age and antibody production within the groups is statistically not significant (Barmen 0.129, Siegburg 0.104, Controls 0.185), and in the absence of immunological evidence that in adults age affects antibody response, this factor seems unlikely to have affected the results. One can, I think, reject the racial difference; the social distress resulting from defeat in war is the essential factor in which the groups differ. Of this social set-up, undernutrition is one factor which has been shown to affect antibody production in animals; therefore, I think it is safe to assume that the difference in antibody production between the groups is mainly due to undernutrition.

Finally, what bearing do these results have upon the problem of epidemic disease? I would draw attention to three points: (1) The extremely severe degree of undernutrition from which the test subjects were suffering—severe enough to render active life impossible; and (2) in spite of this, the comparatively small differences between these literally famished subjects and the controls, in first-class condition; (3) the significant fact that there actually has not been any widespread epidemic disease in Germany since the end of the war. These points taken together suggest that undernutrition does not play as large a part in widespread epidemics as is generally supposed.

This does not dispose of famine as a medical problem, of course, any more than it disposes of it as a human problem; in such signs as a high mortality rate and high incidence of tuberculosis the effect of undernutrition is evident; while the appallingly demoralizing effects of famine constitute a grave psychological problem on their own.

(This work will be published in detail in a Report to the Medical Research Council from the M.R.C. Unit working in Wuppertal.)

Mr. Herbert Parry (Animal Health Trust, Newmarket): Part I^a. *Some of the Variables Involved.*—Any real appraisal of the role played by nutrition in resistance to infection must consider at least four aspects, namely, the host, the nutritional status of the host, the character of the infection and the nature of the resistance, each aspect comprising many variables. The definition of these variables, at first qualitatively and later quantitatively, is essential in dealing with this complicated subject. It is proposed, therefore, to consider in a tentative way some of these variables.

(1) *The host.*—An adequate discussion of this would involve all those factors determining the host's internal environment, cellular and systemic, in which the parasite comes to live. This is obviously impossible, but certain gross determinants, genetic and developmental, must be stressed. The importance of differences between species, and also between different genetic strains within a single breed of a species can be enormous. Results obtained on one strain of a species are not necessarily valid for any other. Hence, it is essential in experimental studies to standardize the genetic constitution of the host animal as far as possible by using highly inbred strains of a given species.

Developmental variation may be equally important, since the age and stage of growth of the animal often plays a decisive role in the outcome of infections. It is well known that young adolescent mice of less than 20 grammes body-weight are much less susceptible to many neurotropic viruses than are older and heavier animals. This phenomenon has been termed "maturation resistance" (Sabin, 1941). If the growth of young mice be retarded by

^aPart II of this paper, *Studies of Total Infections*, will be published in full elsewhere.

restricting food intake or by feeding a diet inadequate for normal growth, such animals retain their "maturation resistance" and are less susceptible to certain experimental infections, although of an age normally fully susceptible. Such lowered susceptibility has been interpreted on occasion as due to some deficiency in the diet. In such instances, unless a control group on a complete diet—but with the food intake precisely similar to that of the deficiency group—be also infected, it is equally possible that the results are due to a continuing "maturation resistance".

(2) *The nutritional situation.*—The nutrition of the host can in part be defined by stating the current consumption of the known nutrients, namely the calories, protein, fat, carbohydrate, the various minerals and accessory dietary factors, but this is not enough. To define the *total nutritional situation* it is necessary to know the previous intake and the reserves of any nutrient, as well as the acuteness or the chronicity of a deficiency of any individual nutrient. Experimentally, individual deficiency states can be produced. In the field, a simple deficiency of one nutrient almost never occurs. We are dealing with adequate and inadequate diets composed of many combinations of individual nutrients in supra-optimal, optimal and sub-optimal amounts, the effects of different nutrients operating in diverse ways, and being often mutually exclusive. Under such conditions it becomes wellnigh impossible to assess the role of nutrition. The experimental approach using diets of highly purified constituents with individual food consumption records and the paired feeding technique seems to offer the only chance of unravelling the tangled skein of conflicting clinical experience. The successful maintenance of animals on such purified diets has made it possible to standardize the nutritional situation.

(3) *The infection.*—Parasitic organisms show so many variations in their effects on a host that to standardize the infection is as important as standardizing the nutritional situation. Detailed consideration of this matter is beyond the scope of this discussion, but suffice it to say that the number of parasitic organisms, their virulence and general biological characteristics within the host, as well as their portal of entry and any auxiliary aids to their establishment, such as trauma or stasis in the alimentary tract, must be defined as precisely as possible.

(4) *Resistance.*—The term resistance has been used to denote so many and various effects that it is increasingly necessary to define what is meant by the term. For the present purpose it is convenient to separate resistance into three levels: first, resistance to the invasion of the parasite through the skin or mucous membranes, *invasion resistance*; second, resistance to the multiplication of the parasite and the accumulation of its pharmacologically active metabolic products in the blood and tissue fluids, i.e. *systemic resistance*; and third, *organ resistance*, resistance to the passage of parasites from the systemic circulation into an organ, and resistance within the organ to any deleterious effects due to the parasites' presence.

(a) *Invasion resistance:* In the main, interest here has been focused on the role of vitamin A in the maintenance of the integrity of ectodermal structures and thereby the resistance of these structures to invasion by parasites. A voluminous and somewhat uncritical literature has grown up which purports to show that the vitamin-A-deficient animal (and man) is more prone to infections of the skin, eyes and alimentary tract. Much of this evidence is in need of a critical reappraisal in the light of recent knowledge.

The role of nutrition in parasitism of the alimentary tract is more clear-cut. There is experimental evidence that a nicotinic-acid-deficient diet will allow the intestinal multiplication and subsequent transmucosal invasion of *Salmonella* in pigs (Chick *et al.*, 1938a, b; Davis *et al.*, 1940) and probably in mice (Watson *et al.*, 1938), while Waisman and Elvehjem (1943) report a diarrhoeic syndrome due to *Shigella paradysenteriae* in monkeys fed a diet deficient in folic acid, and which was controlled by feeding small quantities of folic-acid concentrates.

While the precise reason why these deficient diets should provide conditions suitable for the accumulation of parasites in the bowel is obscure, another group of disorders, the enterotoxæmias of herbivores, are definitely related to the development of local alimentary stasis due to dietary causes, which thereby provide conditions suitable for the rapid multiplication and toxin formation by *Clostridium welchii* (Roberts, 1938).

(b) *Systemic resistance:* Resistance at this level involves many fundamental mechanisms, several of which are to be discussed by other speakers. They will, therefore, only be mentioned very briefly. It is convenient to do so under two heads, first, antiparasitic agencies and, secondly, sensitivity to parasitic toxins.

Antiparasitic agencies include antibody formation, which can be modified by diet; phagocytosis which is limited in the leucopenia of folic-acid deficiency in the monkey; and the absence of metabolites essential for the parasite, a situation more likely to occur in theory than in practice, since the host's requirements are likely to be, in most instances, as critical as those of the parasite.

Sensitivity to toxins, i.e. the size of the mean pharmacological dose, is known to be

influenced in some cases by the nutrition of the host. Thus, diphtheria toxin probably combines with ascorbic acid, and a relative ascorbic-acid deficiency may occur in diphtheria, even when the ascorbic-acid intake is adequate for normal circumstances (King and Menten, 1935; Menten and King, 1935). It is suggested that a very high ascorbic-acid intake may reduce the sensitivity of the host to this toxin, and it is probable that the optimal ascorbic-acid requirement is increased in all fevers. Mice fed on certain mixed diets without skim milk are less resistant to the intraperitoneal inoculation of *Salmonella typhi murium* toxin (Watson, 1937).

(c) *Organ resistance*: The resistance of an organ to an infection embraces two distinct phenomena, *organ entry resistance* and *organ damage resistance*. The former is the resistance to the entry of the parasites, i.e. to their localization, in an organ, the classical example of which is the mechanism of the blood-brain barrier. *Organ damage resistance* may be defined as those factors which limit the damage done to the functional efficiency of the organ by the presence of the invaders or of their metabolic products. Little is known of the factors involved, other than the general mechanisms discussed under systemic resistance, but presumably complex cellular enzyme systems are also involved. There are suggestions of this in the work of the Wisconsin school on the role of thiamine in determining the development of functional defects of the nervous system due to some neurotropic viruses (see Rasmussen *et al.*, 1944).

(d) *Criteria of resistance*: So many criteria of increased resistance have been employed, including lengthening of the incubation period, lessened severity of the local signs of organ damage, the shortening of the duration of clinical signs, reduced numbers of deaths, reduced numbers of viable organisms as determined by laboratory tests, more rapidly produced or higher antibody titres, and others. Many of these criteria embrace different aspects of invasion, systemic and organ resistance. Unless due regard be paid to these differences when selecting criteria there seems little chance that the true role of nutrition in resistance to infections will be elucidated. Of the many possible criteria, one of the simplest is the development of functional defects in the central nervous system following infections with the neurotropic viruses, which involves in particular organ resistance. In the hands of Clark and his colleagues (see Rasmussen *et al.*, 1944) the retardation of the development of paralysis of the hind-limbs in infected animals has proved a valuable quantitative criterion of resistance.

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Dr. Z. A. Leitner: When bacteria or their products enter the body they are gradually removed by the "clearing mechanism" consisting mainly of the wandering cells of the reticulo-endothelial system [5]. Soon afterwards "shedding" of fragments of the superficial cytoplasm layers of these cells occurs and coincides with the appearance of antibodies [11] and with an increase of gamma globulins [6]. The cells forming the gamma globulins appear to be sensitized and they seem to synthesize antibody globulin more rapidly than normal cells when exogenous protein gains access to them [11]. Moreover, in dogs depleted of proteins by inadequate diet or plasmaphoresis, the replenishment of antibody globulin depends on supply of dietary protein after exhaustion of the "reserve bank" of intracellular proteins [12]. Sufficient amount of dietary protein seems, therefore, to be as essential for adequate synthesis of antibodies as their proper absorption from the intestine and the conversion of amino-acids into plasma proteins in the liver. Interference with any of these functions may lead to hypoproteinaemia and infections (e.g. in liver cirrhosis).

Avitaminoses, especially those due to vitamin-A, -C and -D deficiency, are also said to reduce natural resistance. Conflicting views about the relationship of vitamin deficiency to infection appear to be due partially to the varying definition of the deficiency itself [7]. Whilst in cases of vitamin deficiency administration of the missing vitamin may help to restore normal resistance, such vitamin therapy does not increase resistance or immunity in normal persons.

Vitamin-A deficiency causes an atrophy of the epithelial surfaces followed by keratinizing metaplasia and a lowered local resistance. This may partly explain a variety of infections in

animals [3] and also in children [2]. A more satisfactory explanation cannot be advanced yet as to the mechanism of decreased general resistance in vitamin-A deficiency; it does not appear to be due to diminished antibody production though vitamin-A deficiency may interfere with the efficient action of natural antibodies, especially in children [1, 4].

Results of an investigation carried out by the author with Drs. Jacobs, Moore, Sharman and Thornton during the last four years on the relation of vitamin A to certain infections were briefly discussed. Tables demonstrating the carotene and vitamin-A values in normal persons [8, 9] and, as a comparison, the considerably lowered vitamin-A values in patients suffering from pleurisy, pneumonia and especially from rheumatic fever were shown [10]. A guarded indication for prognosis was put forward on account of some observations made during the recovery period in rheumatism. The curves presented seemed to indicate that there was no recurrence after the first attack in patients with high vitamin-A level; other cases with apparently complete clinical recovery and normal E.S.R. but with low blood vitamin-A level had repeated relapses during the observation period. A warning against generalization from these preliminary observations was added and the hope expressed that they might contribute to further elucidation of the relationship of certain nutritional factors to infection, particularly in rheumatic fever.

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Dr. J. W. Howie said that fifteen months ago the Rowett Research Institute, Aberdeen, adopted work on nutrition and resistance to infection as part of its programme, and he spoke for a team of workers now engaged on the subject. Observations were being made on the immunity responses of calorie- and protein-deficient ewes. The immunity response was not always a true index of capacity to resist infection; therefore it seemed most useful to study the type of antibody best established as a factor in resistance. For this reason, with the collaboration of Mrs. I. Batty, of the Wellcome Research Laboratories, the antibody under investigation was *Clostridium welchii* β antitoxin. It was possible to say only that at this stage of the work and with the particular scheme of immunization employed the calorie- and protein-deficient ewes had produced more antitoxin than the well-fed control animals; details of the experiment would not be reported until it was complete, and the final picture might be quite different.

Mice on different diets were also being tested by noting the survival rates after infection with a variety of agents including Salmonella, louping-ill virus, and tubercle bacilli. A colony of white Swiss mice had been established and in consequence of rigid precautions it had been kept free from spontaneous Salmonella infection for one year. Thus it was possible to design experiments in which the test and control animals were alike in age, sex, and heredity and differed only in their diets. It was well known, and had been confirmed, that some diets influenced resistance to infection only in the next generation. In one experiment raising the proportion of casein in the diet without increasing the calories had resulted in greater resistance in young male mice to Salmonella infection by mouth, but the resistance of young female mice had not been influenced by the same procedure. The experimental diet was unsatisfactory for reproduction and rearing and the experiment was being repeated with what he hoped might prove a more satisfactory diet.

Other experiments were also in progress at the Institute on the effect of a protein-rich supplement on the worm burdens of ewes and their lambs; on antibody production in pyridoxin-deficient rats; and on nutritional and other environmental factors likely to influence the resistance of young pigs to infection.

The problems were attractive, as might be judged by the numerous publications on the subject, but clear answers to most questions about nutrition and resistance to infection were still lacking, as Schneider (1946) had demonstrated.

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Sir Percival Hartley said that, in his studies of the factors affecting antibody production, prominence had been given to the effect of nutrition. Experiments had been carried out on guinea-pigs and included the three main phases of their immunization history—the response to the primary and secondary stimulus, respectively, and the quiescent period between these events. The antigens used were diphtheria toxoid and alum-precipitated toxoid, the diphtheria antitoxin produced was precisely measured, and the state of nutrition varied by adjusting the amount of cabbage fed daily to the animals.

Response to the primary stimulus was markedly affected by diet. Fifteen guinea-pigs given an adequate diet grew well, all survived and gave an excellent antibody response; an exactly similar group given mangolds in place of cabbage did not grow, four of them died, and the survivors gave a poor antibody response [1]. By using groups of 50 guinea-pigs it was shown that animals given 50 grammes of cabbage daily produced a significantly larger amount of antitoxin than those given 20 grammes daily. When 13 immunized guinea-pigs were deprived of cabbage for twenty-one days, there was no change in the antitoxin level in 5 and a slight decline occurred in 8. The cabbage-free diet being continued, these 13 guinea-pigs were given the same dose of antigen as 12 similarly immunized guinea-pigs which had been maintained constantly on an adequate diet. Of the diet-restricted group 5 died on or before the fifth day following the injection of antigen, all of these showing, at post-mortem, characteristic symptoms of undernutrition; but each of the remaining 8 showed a rise in antitoxin titre although it was small compared with that produced by the adequately fed control group. This severe and prolonged deprivation of cabbage was the only condition which affected, significantly, the response to the secondary stimulus; if the restriction was continued for one week only no decline in response occurred [2]. Neither exposure to cold, intercurrent infection persisting throughout the period of the secondary response, a continued condition of tetanus, produced by the injection of a sublethal dose of tetanus toxin and maintained during the whole period of the secondary response, nor intravenous injections of Indian ink made any significant difference to the response to the secondary stimulus. In all the experiments the antigens had been quantitatively investigated before use and, as the charts showed, the doses injected were sufficiently small to permit of the submaximal effects produced being quantitatively estimated and compared.

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[February 18, 1948]

DISCUSSION ON SWINE ERYSIPELAS INFECTION (*ERYSIPELOTHRIX RHUSIOPATHIÆ*) IN MAN AND ANIMALS

Dr. Mary Barber: *Erysipelothrix infection in man.*—The bacillus of swine erysipelas is either pathogenic or saprophytic throughout the animal kingdom. It can survive in dead matter of animal or plant origin for a very long time and is extremely resistant to salting or putrefaction. Compared with swine, man is relatively immune to infection with this organism. Three types of infection have, however, been described in man, cutaneous, intestinal and generalized; the first type, referred to as erysipeloid of Rosenbach being by far the most common.

ERYSIPELOID OF ROSENBACH

Fox gave what is probably the first description of a single case of this condition in the *British Medical Journal* in 1870. In 1873, Baker, in the *St. Bartholomew's Hospital Reports*, gave an interesting study of 16 cases of a similar condition, which he called erythema serpens. He observed that there was usually a history of injury a few days to a week before the onset; in 6 of his cases the condition followed a scratch by a bone or a cut while handling meat or rabbit skins and one followed a dog bite. He stated that the disease spread leaving "one portion sound as it involves another". The site of injury never showed any signs of infection. The erythema itself never suppurated and there was no inflammation of veins or lymphatics. The prognosis was always favourable, all cases clearing up in two to six weeks.

The classical studies of Rosenbach (1884 *et seq.*) not only established the disease as a clinical entity but proved its causal relationship with swine erysipelas. His description of the skin lesions has not been improved upon. In 1887 he described them as erysipelas-like, slowly progressive, sharply defined, slightly elevated, dark, violaceous, almost livid red zones. He observed, as Baker had done, that the central area of redness faded as the disease extended peripherally. In this same paper he describes the organism which he isolated from a skin biopsy of one patient. He said it was larger than a staphylococcus and in older cultures became a mass of branching threads. He injected a pure culture of it into his own arm and

produced a typical erysipeloid lesion. In a paper in 1909 he compared organisms isolated respectively from swine erysipelas, mouse sepsis and erysipeloid lesions in man. He found them serologically and "toxically" similar, but thought they were distinct morphologically and culturally. Felsenthal in 1893 also recovered an organism from skin biopsies of 3 out of 4 patients with erysipeloid and noted its resemblance to the causal organism of swine erysipelas.

Epidemiology.—The condition is met fairly frequently in any large skin clinic, but as a rule the diagnosis is not confirmed bacteriologically. Most of the cases are cooks, kitchen workers, butchers or people who handle fish, and they occur most frequently between the months of May and September. Klauder (1938) analysed the source of infection in 100 cases. In all, contact with dead animal matter could be traced; in 58, who were abattoir workers, the infection was from swine and in 16 it was from fish.

Clinical features.—The incubation period is in most cases one to five days. The disease is confined almost exclusively to the hand, starting in most cases at the site of the puncture wound and rarely progresses above the wrist. A few cases, where the lesion was on the soles of the feet, face or neck, have been recorded. The patient complains of a sensation of burning, pricking, itching and pain; occasionally the pain is severe, it may radiate up the arm. The surface of the erythematous areas remains smooth, no papules, vesicles or other lesions appear. The most distinctive features are the purplish-red colour and the well-defined margin. Another characteristic sign is that the central area of redness fades as the disease spreads peripherally.

Lymphangitis and glandular enlargement are rare and suppuration has never been recorded. In most cases fever and constitutional symptoms are slight or absent. The lesions disappear spontaneously in from five days to about six weeks, without desquamation. Recurrences, however, are not infrequent.

Diagnosis.—The clinical picture is characteristic and the diagnosis often rests on this alone. Bacteriological confirmation is difficult. It is usually only possible to isolate the organism if an actual biopsy of skin is taken and even then it is not always easy. Of 7 cases admitted to Hammersmith Hospital in the summer of 1945, skin biopsies were cultured from all, but from five only was the organism isolated (see Barber, Nellen and Zoob, 1946). In this localized form of the disease no detectable agglutinins to *E. rhusiopathiæ* appear in the patient's blood stream. Biberstein (1933) described an intracutaneous test using filtrates from cultures of *E. rhusiopathiæ*. He claimed that filtrates from ten-day-old cultures gave 88% of positive results in 17 cases of active erysipeloid; 5% of 60 normal people, however, also gave a positive result.

Treatment.—The assessment of treatment in a disease which is naturally self-limited is difficult. Prior to the introduction of modern chemotherapeutic drugs serum was the usual method and it was claimed to be beneficial. The effect of sulphonamide compounds is disputed. Klauder and Rule (1944) stated that these drugs had no effect on erysipeloid lesions in man and they showed that they had little or no effect on experimental infection of mice with *E. rhusiopathiæ*. Schoch and Shelmire (1940) and Kulchar and Rosenberg (1941) on the other hand claim that sulphonamide therapy has a curative effect on erysipeloid eruptions. Few cases treated with penicillin have so far been recorded, but Heilman and Herrell (1944) have shown that this compound is curative in experimental infection in mice. I myself have observed 1 case treated with penicillin and the effect was dramatic (Barber, Nellen and Zoob, 1946).

Histology.—The histological appearance is not characteristic. Düttmann (1921) has demonstrated that the organisms are usually in the deep part of the pars reticularis of the corium. He therefore points out the necessity for excising deeply for bacteriological studies.

SEPTICÆMIA AND ENDOCARDITIS

Blood-stream infection with *E. rhusiopathiæ* in man is rare. A few cases have however been recorded. Gunther in 1912 reported 2 cases occurring in veterinarians accidentally inoculated with a culture, but these cases were not studied bacteriologically. Prausnitz in 1921 described a child of 10 with a clinical picture of septicæmia and endocarditis from whom *E. rhusiopathiæ* was grown from the blood but no post-mortem examination was performed. The first case of Erysipelothrix infection leading to endocarditis proved bacteriologically and at post mortem was described by Russell and Lamb (1940). There were no skin lesions; the heart was enlarged and there was a systolic thrill and murmur at the base. *E. rhusiopathiæ* was isolated from the blood on six occasions. The patient died a month after admission to hospital in spite of treatment with sulphanilamide. Post mortem the heart was nearly twice normal size, there were three small pinkish-yellow granular firmly adherent vegetations on the anterior cusp of the mitral valve, and the aortic cusps, only two in number, were largely replaced by fungating, friable vegetations.

Klauder *et al.* (1943) reported the condition in a butcher with a history that five months previously his left thumb had been lacerated with a meat bone. This was followed in three days by extensive acute inflammation of the thumb, so severe that one physician recommended amputation. However, complete recovery eventually took place and he returned to work two months after the injury and worked regularly until two months later he felt weak and sick and retired to bed. At this time he had fever and a purpuric eruption. A month later he was admitted to hospital, where he died six months after the original injury in spite of full doses of sulphathiazole.

Blood-count revealed a normochromic anæmia. *E. rhusiopathiæ* was isolated from the blood on three occasions. Post mortem a friable vegetation $\frac{1}{4}$ in. in diameter was present on one aortic cusp.

Infection via alimentary tract.—One case has been reported by Fiessinger and Brouet (1934) in whom infection followed the ingestion of salt pork.

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Mr. A. W. Gledhill (*Institute of Animal Pathology, University of Cambridge*): *Erysipelothrix rhusiopathiæ* was identified as the causative organism of swine erysipelas by Löffler in 1885. Losses from the disease have perhaps been most heavy in the Continent of Europe. In Britain it is prevalent in East Anglia where on some farms it would be almost impossible to raise pigs without recourse to vaccination and treatment with immune serum; yet in some other parts of Britain it is quite uncommon.

Erysipelothrix rhusiopathiæ occurs fairly commonly in birds of most species usually causing sporadic deaths, although quite extensive outbreaks among birds have been attributed to it. The organism is also a common cause of arthritis in lambs (Poels, 1913; Christiansen, 1919; Cornell and Glover, 1925), and endocarditis in horses (Paterson and Heatley, 1938).

Formerly, the pig was regarded as being the natural host of *E. rhusiopathiæ*, swine erysipelas and human erysipeloid being supposed to result exclusively from direct or indirect contact with affected pigs. Evidence has, however, accumulated to show that *E. rhusiopathiæ* can live as a harmless saprophyte. The organism has been recovered from the slime of fish, from houseflies and from putrefying matter (Heilman and Herrell, 1944). It can live saprophically in the intestines and tonsils of pigs and this is no doubt true of other species of animals. Six strains of high virulence were recovered from the tonsils of 50 pigs (Bramm, 1937). On other occasions workers have failed to recover the organism from normal pigs (Huytra and Marek, 1920). This difference probably depends upon the locality to which the pigs belonged. Probably this accounts for the fact that in districts where the disease occurs the sera of animals having no history of clinical infection often contain both agglutinins and antibodies capable of protecting mice passively against infection with *E. rhusiopathiæ*. I have observed a rise and fall of agglutinins in sera from horses over a period of several months. Furthermore, three sera from a batch of five similar normal pigs bred at the Institute of Animal Pathology, Cambridge, protected mice against lethal infection with *E. rhusiopathiæ*. Of the two remaining sera, one lengthened the life of the test mice a little, while the other had no effect at all. It was also observed that the serum and precolostrum of a cow had agglutinating titres of 1:40 and 1:160 respectively and that the precolostrum protected mice. If it can be assumed that specific antibodies are concerned with these agglutination and mouse protection results, it would seem that in areas where the disease occurs subclinical infections are common. The active immunity engendered by these perhaps explains the difficulty in producing swine erysipelas by injecting pigs with virulent cultures. Pigs between the ages of 3 months and 1 year are most susceptible. No doubt sucking pigs receive protective anti-

bodies from the sow, whilst pigs over a year of age may have usually acquired sufficient active immunity to resist infection. But the existence of a low-grade active immunity makes it difficult to understand how the majority of young weaned pigs in such districts can become highly susceptible to natural infection, usually in the hot summer months. Whether the emergence of enzootic swine erysipelas is due to a lowered resistance in the pig population or to a sudden rise in virulence of the organism is not known. The virulence of strains of *E. rhusiopathiae* is certainly an unstable entity which can often be raised experimentally.

Three forms of swine erysipelas are recognized in pigs, the mild form characterized by urticaria, the acute septicæmic form and the chronic form, characterized by vegetative endocarditis. It is generally supposed that the acute disease is a septicæmia and that the mild and chronic diseases are preceded by a transient septicæmia before localization of the organisms in the skin, the joints or the endocardium. It was, however, suggested by some early workers that *in vivo* *E. rhusiopathiae* produces an extra-cellular toxin. Thus, the acute disease would be essentially a general toxæmia whilst the urticaria and endocarditis of mild and chronic erysipelas would be due to invasion of the affected tissues by organisms. This view received some support by the observation that after cutaneous inoculation pigs sometimes become fatally affected with symptoms of erysipelas although the bacilli are found only at the point of inoculation and in its immediate vicinity (Hutyra and Marek, 1920). Moreover, "Voges and Schutz (1898) showed that after inoculation with the second Pasteurian vaccine, and after simultaneous injection of antiserum and living virus (sero-vaccination), the blood of pigs was teeming with bacilli, which, nevertheless, caused no visible disturbance in the pigs; Prettnner (1906) found that passively immunized mice harboured virulent infection in their tissues for twenty-four hours to three days after inoculation of culture" (M.R.C. System of Bacteriology, 1931). I have observed that mice, passively protected against the immediate effects of several thousand lethal doses of virulent culture, will often succumb to acute infection several weeks later, especially if subjected to strain. These observations support the view that immune serum acts by neutralizing the toxic effect of *Erysipelothrix* organisms rather than by promoting their destruction. This would seem to imply that the organisms produce a neutralizable toxin *in vivo*. The hypothesis that such a toxin is produced might explain why an organism sensitive to about 0.1 unit of penicillin per ml. yet requires 1,000 units per mouse per day to achieve 95% protection (Heilman and Herrell, 1944; Woodbine, 1946, 1947). This raises the question of curative treatment.

Treatment.—Immune serum in liberal doses has a curative action upon the acute disease in pigs. In man it is also alleged to have a curative action but not infrequently it appears to produce a type of serum sickness more incapacitating than erysipeloid itself. In birds, it has not consistently produced good results (Vianello, 1938; Graham, Levine and Hester, 1939). As curative agents the sulphonamides are not of value (Woodbine, 1946). As already stated, the organism is sensitive to penicillin *in vitro*. To a less extent it is also sensitive to streptomycin. In man a number of instances of the success of penicillin therapy have been published. Upon the hypothesis that the acute fatal infection of mice and pigs is due to a toxin, one might expect greater success in the case of man in whom acute general symptoms are not a regular feature of the disease. Similarly in pigs one might perhaps expect poor results from penicillin therapy in the acute form while the chronic form might be more amenable to treatment. I have not seen any reports of the use of penicillin in pigs. Indeed, it would be difficult to arrange an adequate trial bearing in mind that the disease has not been produced experimentally with any regularity and that pigs affected with the natural disease are treated with immune serum. In the case of the chronic type, the diagnosis is generally established with certainty only post mortem.

Prevention.—The usual method of prophylactic immunization is by inoculating subcutaneously viable culture and immune serum followed by culture alone a week or so later. Satisfactory results are obtained by this method. It does, however, present disadvantages. In the first place, hyperimmune horse serum is expensive and difficult to produce in sufficient quantities to meet the needs of some countries, in particular the Central European countries. Secondly, there are the dangers accruing to the use of fully virulent viable viruses as immunizing agents.

To avoid the use of hyperimmune serum, attenuated viable cultures have been used, e.g. the rabbit-passaged material elaborated by Pasteur. It does not appear to me that the hope of producing a more stable attenuated culture is very well founded. Recently, I obtained from Mr. T. M. Doyle of the Ministry of Agriculture Laboratory, Weybridge, a strain capable of immunizing mice without producing symptoms in them. After subculturing this strain in series daily in 10% pig serum broth and in glucose broth for about a fortnight, the former culture inoculated intraperitoneally was capable of making mice ill. By culturing from the sick mice into the same medium and repeating the operation, the third and fourth mouse passage killed mice in two to three days. The culture was then maintained in pig

serum broth and in due course its virulence determined. It was now capable of killing mice at high dilution although it took longer to kill than would a really virulent culture. It was also shown *in vitro* that the treatment had induced a power in the culture not possessed at first. As shown elsewhere smooth strains of *Erysipelothrix rhusiopathiae* produce an antigenic component when grown in serum media which is not produced in the absence of serum (Gledhill, 1947). This was demonstrated by absorbing with organisms grown in serum-free media an immune rabbit serum produced against the same strain grown in serum media. At first such an absorbed serum did not agglutinate suspensions grown in serum media of the strain in question. However, after the strain had become capable of killing mice it was agglutinated by the absorbed serum at a dilution of 1 : 160, the titre of the absorbed serum with the homologous strain. One can easily imagine natural conditions in which could occur a similar rise in virulence of an avirulent strain as that described here.

The ideal method of immunization is clearly by means of inactivated organisms or by antigenic substances derived from them. Heat-killed cultures are valueless for this purpose. Moreover, it has been shown that merthiolate-killed organisms grown in media not containing serum do not produce immune sera in rabbits (Gledhill, 1945). However, organisms grown in media containing horse serum and similarly killed do produce immune sera in rabbits. To determine experimentally whether such a vaccine would immunize pigs presents the difficulty that pigs are not generally susceptible to artificial infection. In collaboration with Mr. J. A. J. Venn of the Institute of Animal Pathology, Cambridge, I have sought to determine the degree to which vaccines raise the immune bodies in pigs' sera by estimating their capacity to protect mice against infection. As a standard to be attained by vaccines, we have taken the power to protect mice of the sera of pigs immunized with viable culture by the recognized method. Killed organisms grown in serum broth inoculated subcutaneously produced no response, while intravenously the response was insufficient. It has since been found that the cell-free serum broth in which the organism has grown for eighteen to twenty hours is antigenic and the use of this would seem to promise more success in pigs, especially if the fowl is used as the source of serum in the medium (Table I).

TABLE I.—AGENTS PRODUCING IMMUNE BODIES IN SERA OF PIGS

Pig No.	Agent used for immunizing pig	Route of inoculation	Doses injected ml.	Dose of serum given to mice ml.	No. of mice which died
1	Viable culture	s/c	1.0, 1.0	0.1	5/10
2	Supernatant of centrifuged horse serum broth culture	i/v	5, 10, 20, 20	0.1	4/6
3	Supernatant of centrifuged fowl serum broth culture	i/v	2, 4, 6, 6	0.1	1/6
3	Before immunization. None	—	—	0.3	6/6

Infecting dose : 100,000 virulent bacilli given intraperitoneally 24 hours after serum.

Traub (1947) and also Dinter and Bakos (1948) have shown to be present in culture media an antigen capable of immunizing pigs against swine erysipelas. Our observations indicate that the antigen free in the medium resembles that produced on the organism by growth in serum media in the following particulars: (1) Both are produced only in the presence of serum in the medium. (2) Both are thermolabile, being destroyed by heating to 55° C. for thirty minutes. (3) A serum produced in the rabbit against the antigen free in the medium was much reduced in efficacy for protecting mice by absorption with organisms.

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Section of Epidemiology and State Medicine

President—W. S. C. COPEMAN, O.B.E., F.R.C.P.

[January 5, 1948]

A Statistical Analysis of Geriatric Care

By L. COSIN, F.R.C.S.

PUBLIC Health and State Medicine, having concerned themselves with the prevention of many of the epidemic causes of death during the last hundred years, must now turn to the situation produced by the success of such a policy.

I shall not mention many figures to indicate the size of the problem except to point out that the number of people of pensionable age will exceed 9,000,000 in twenty years' time; in 1946 the number was 6½ million. The average expectation of life at birth to-day is about 62 in men and 67 in women, while the average morbidity of people over the age of 60 is at least five times that of the population of all ages. Faced with an increasing shortage of nurses and the great increase in the number of elderly invalids, a breakdown in our hospital system is likely unless the problem about to be discussed is solved. Before considering a solution, however, we must ascertain the amount of nursing attention required for the average elderly patient who becomes hospitalized. Although there must be many other correlated factors influencing the hospital stay of ageing patients, the chief are: (1) Type of case admitted. (2) Efficiency of medical and surgical treatment. (3) Amount of rehabilitation provided. (4) Amount of treatment, before admission, which may depend upon the length of the waiting list.

The length of the waiting list is dependent upon the following factors: (1) The size of the hospital. (2) The number of available beds for this type of patient. (3) The varying scarcity of nursing staffs. (4) The size of the aged population in the locality. (5) The patient's social position, which largely determines his ability, or inability, to obtain suitable socio-medical attention, although this is becoming less absolute in its application. (6) The attitude of most voluntary and many municipal hospitals to this type of patient.

Dependent upon these factors are the deplorably late admissions in the natural history of the disease, which may have an effect in shortening hospital stay by an increased death-rate, and the failure of many aged patients to gain admission at all. The use of antibiotics, chemotherapy and cardiac diuretics will also tend to increase the length of hospital stay.

The only figure available for average length of stay of elderly sick appears to be that of 260 days for 1938 quoted by Dr. J. Cohen in the Working Party's Report on the Nursing Profession. Using this figure as a standard of comparison, which is probably still true in many institutions, we can examine some figures from the Orsett Lodge Hospital in the Essex County Council's Social Welfare and Hospital Service. The reopening of the hospital on 7.11.44 for civilian patients after war closure permitted us to survey the results of geriatric rehabilitation over the following twenty-six months until 10.1.47 when the reduction of the nursing staff to 26 determined the closure of 60 beds in two wards.

An active attempt was made to diagnose, classify and treat this neglected type of patient as fully as possible. During the first part of the period under review, treatment was based on routine medicine, surgery and physiotherapy. Our medical and surgical care was producing gratifying results in the diminution of the death-rate but the failure at first to rehabilitate as many elderly patients as possible produced its own bottleneck.

SOURCES OF PATIENTS

During the period under survey—November 1944 to January 1947—Orsett Lodge Hospital, a Social Welfare Institution in a South Essex industrial area, drew its elderly patients from:

- (1) The 23 old people left of the patients not evacuated.
- (2) The return of 91 elderly people in November 1944 and 97 more in March 1945, some 50 of whom were originally from other hospitals.

I think it has been a frequent experience that old patients evacuated during the war were too often allowed to become bedfast instead of being kept ambulant. This may have been due to the nursing and other shortages; however, the rehabilitation of the bulk of these patients, some three-quarters of whom were bedfast, became an important problem.

- (3) The elderly people admitted from the local area, very often after a long period on the waiting list.

(4) The victims of senile confusional states admitted because of the inability of the local mental hospitals to admit all patients of this type.

- (5) Elderly patients from the East London metropolitan area of Barking, Ilford, Romford and Dagenham.

(6) Elderly patients from that part of the north bank of the Thames stretching from East London to Canvey Island, about 35 miles.

serum broth and in due course its virulence determined. It was now capable of killing mice at high dilution although it took longer to kill than would a really virulent culture. It was also shown *in vitro* that the treatment had induced a power in the culture not possessed at first. As shown elsewhere smooth strains of *Erysipelothrix rhusiopathiae* produce an antigenic component when grown in serum media which is not produced in the absence of serum (Gledhill, 1947). This was demonstrated by absorbing with organisms grown in serum-free media an immune rabbit serum produced against the same strain grown in serum media. At first such an absorbed serum did not agglutinate suspensions grown in serum media of the strain in question. However, after the strain had become capable of killing mice it was agglutinated by the absorbed serum at a dilution of 1:160, the titre of the absorbed serum with the homologous strain. One can easily imagine natural conditions in which could occur a similar rise in virulence of an avirulent strain as that described here.

The ideal method of immunization is clearly by means of inactivated organisms or by antigenic substances derived from them. Heat-killed cultures are valueless for this purpose. Moreover, it has been shown that merthiolate-killed organisms grown in media not containing serum do not produce immune sera in rabbits (Gledhill, 1945). However, organisms grown in media containing horse serum and similarly killed do produce immune sera in rabbits. To determine experimentally whether such a vaccine would immunize pigs presents the difficulty that pigs are not generally susceptible to artificial infection. In collaboration with Mr. J. A. J. Venn of the Institute of Animal Pathology, Cambridge, I have sought to determine the degree to which vaccines raise the immune bodies in pigs' sera by estimating their capacity to protect mice against infection. As a standard to be attained by vaccines, we have taken the power to protect mice of the sera of pigs immunized with viable culture by the recognized method. Killed organisms grown in serum broth inoculated subcutaneously produced no response, while intravenously the response was insufficient. It has since been found that the cell-free serum broth in which the organism has grown for eighteen to twenty hours is antigenic and the use of this would seem to promise more success in pigs, especially if the fowl is used as the source of serum in the medium (Table I).

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Pig No.	Agent used for immunizing pig	Route of inoculation	Doses injected ml.	Dose of serum given to mice ml.	No. of mice which died
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3	Before immunization. None	—	—	0.3	6/6

Infecting dose: 100,000 virulent bacilli given intraperitoneally 24 hours after serum.

Traub (1947) and also Dinter and Bakos (1948) have shown to be present in culture media an antigen capable of immunizing pigs against swine erysipelas. Our observations indicate that the antigen free in the medium resembles that produced on the organism by growth in serum media in the following particulars: (1) Both are produced only in the presence of serum in the medium. (2) Both are thermolabile, being destroyed by heating to 55° C. for thirty minutes. (3) A serum produced in the rabbit against the antigen free in the medium was much reduced in efficacy for protecting mice by absorption with organisms.

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ANALYSIS OF DEATHS—M. 170, W. 126

Treatment period			Treatment period		
1-7 days	M. 51 W. 26	} 77	91-180 days	M. 16 W. 19	} 35
8-30 days	M. 38 W. 36		181-365 days	M. 7 W. 14	
31-90 days	M. 37 W. 28	} 65	Over one year	M. 21 W. 3	} 24
Total	296			

I will return, after completing the analysis of patients in hospital on 10.1.47, to the problem of the long-stay patient.

TABLE IIA.—ANALYSIS OF RESIDENTS 10.1.47

Active Treatment or Bedfast M. 30, W. 29.

Duration of Treatment			Duration of Treatment		
1-7 days	M. 2 W. 1	} 3	91-180 days	M. 3 W. 2	} 5
8-30 days	M. 2 W. 3		181-365 days	M. 4 W. 4	
31-90 days	M. 6 W. 5	} 11	Over one year	M. 13 W. 14	} 27
Total	59 (8%)			

On 10.1.47 there were 59 patients in bed, of whom 35 can be considered as permanently bedfast, roughly 4% of the total; to this, however, must be added 45 long-term patients who had died after a longer hospital bedfast stay than six months. The total of 80, or about 10% then, is a fair estimate of the problem of nursing the long-stay permanently bedfast cases. The 1947 figures, which were card-indexed and very accurately surveyed by Mr. W. H. Leak, the County Statistical Officer, show that under 10% were permanently bedfast (i.e. over six months).

TABLE IIB.—ANALYSIS OF RESIDENTS 10.1.47

Long-Stay Annexe Residents M. 65, W. 42.

1-7 days	M. 0 W. 0	} 0	91-180 days	M. 3 W. 5	} 8
8-30 days	M. 0 W. 5		181-365 days	M. 16 W. 5	
31-90 days	M. 5 W. 3	} 8	Over one year	M. 41 W. 24	} 65
Total	107 (14%)			

The long-stay annexe residents are rehabilitated patients who are either capable of looking after themselves without any assistance (long-stay annexe for the ambulant) or are in need of extra physical help (long-stay annexe for the frail ambulant). The common feature, however, is the fact that there is no need for a full-time nursing service which would be essential if the patients were bedfast in acute geriatric wards or in a long-stay annexe for the permanently bedfast.

The lengths of stay (Table IIB) comprise both the period in the acute geriatric wards and the long-stay annexes. The mean figure of 51.6 days before discharge could reasonably be used as an index of length of stay in the acute geriatric ward before transfer to the long-stay annexes.

LONG-STAY CASES

Pursuing the problem of the long-stay cases, I have followed up the 166 patients who were in hospital on 10.1.47 to 31.12.47 (Tables III and IV).

TABLE III.—ANALYSIS OF ADMISSIONS BEFORE 10.1.47 MADE ON 31.12.47

	Men	Women	Total
Discharged ..	11	7	18
Transfers ..	2	2	4
Deaths ..	26	18	44
Long-stay annexes	50	31	81
Bed ..	4	15	19

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TABLE IV.—DISCHARGES DURING 1947

Length of stay	Women	Men	
0-30 ..	—	—	} 11
31-90 ..	5	4	
91-180 ..	—	5	
181-365 ..	—	1	
Over one year	2	1	

Total 18

The number of deaths (44) (Table V) is very interesting because, first they take the total death-rate for the period 7.11.44 to 31.12.47 up to $296 \div 44 = 340$ or 43%, and secondly I have been able to divide them into two categories. 16 of the deaths occurred in patients who had been permanently bedfast over six months for the whole period of hospital stay—that is up to three years, but the new factor of 20 or over half of the long-term deaths occurred in geriatric wards after residence in long-stay annexes. It appears that a large proportion of patients in long-stay annexes for reasons of physical infirmity or social need will have only a short final illness.

(7) Some subjects of surgical emergencies of all ages, including the elderly, from a similar area.

(8) Transfers from other hospitals because of a hopeless prognosis.

The total number of admissions of patients over the age of 60 for this period of twenty-six months amounted to about 780, while the number of patients under that age amounted to about 650, excluding maternity patients. About 200 of the 780 cases were already of the long-stay hospital type admitted during the first part of the period.

RESULTS OF TREATMENT

As much of the analysis was carried out after the end of the period it was not possible to card-index all admissions, as has been done in 1947, but a separate sheet of each month's admissions was prepared for each sex, showing name, age, date of admission and one column each for the date of discharge, death or transfer. A final column was provided to indicate length of stay. In all cases the length of stay has been assumed to be the period of bedfast days.

I have referred to the fact that the analysis was carried out in retrospect and it has not been possible to attain 100% accuracy. This is reflected in the admissions, combined with those ageing patients resident before November 7, 1944, amounting to three less than the combined figure for deaths, discharges, transfers and residents on January 10, 1947. As several patients were readmitted, sometimes on more than one occasion, this probably accounts for an error which is less than 0.4% (Table I).

Results of Treatment of Patients Over 60 Admitted Between 7.11.44 and 10.1.47				Admissions 7.11.44 to 10.1.47		Average Duration of Stay in Days of Elderly Patients Admitted Between 7.11.44 and 10.1.47		
						Death	Discharge	Transfer
Transferred	M. 16 } W. 19 }	35	4%	M. 438 } W. 317 }	755	Men 92.2	53.6	270.1
Discharged	M. 177 } W. 107 }	284	37%	Resident 6.11.44		Women 82.2	49.2	206.9
Died	M. 170 } W. 126 }	296	38%	M. 20 } W. 3 }	23	87.6	51.6	235.0
Resident 10.1.47	M. 95 } W. 71 }	166	21%			I am grateful to Dr. Cohen, of the Cabinet Office, for providing the statistical figures of average length of stay.		

The transfers amount to 35 or 4% of the total. The usual causes of transference are lunacy certification, and those patients needing radium, deep X-ray or thoracic surgery, which are not available at this hospital. On this occasion, however, 15 from a long-stay annexe were accounted for by their transfer in July 1946 to another Essex County Council hospital as a result of the war evacuation, which explains the high average length of stay. Probably a 2% transfer rate is more usual.

The total number of patients discharged amounts to 284 or 37% of the total. This represents a large batch of rehabilitated elderly patients: others will be found in an analysis of patients in hospital on 10.1.47 (Table II A and B) as 107 (14% of the total) were in long-stay annexes for ambulant or frail ambulant cases. This brings the total number of rehabilitated elderly up to 51%.

ANALYSIS OF DISCHARGES—M. 177, W. 107

Treatment period			Treatment period		
1-7 days	M. 32 } W. 12 }	44	91-180 days	M. 18 } W. 7 }	25
8-30 days	M. 56 } W. 41 }	97	181-365 days	M. 10 } W. 6 }	16
31-90 days	M. 58 } W. 40 }	98	Over one year	M. 3 } W. 1 }	4
Total	..	284			

It will be seen that 239 or over 80% of these patients were discharged under three months, while another 41 were discharged in under one year.

As this analysis was over a two-year period it is reasonable to assume that recovery should be completed in less than one year, but only six months should be required for about 90% of the cases.

On turning to the deaths it was found that there were 296 out of 781, making a percentage of 38. The interesting fact here is that 73% or nearly three-quarters of the deaths occurred in less than three months after admission to hospital, that 85% of the deaths had taken place in less than six months, while 8% of them, or 3% of the total admissions, took place between twelve and twenty-six months.

Old Age in General Practice

By TREVOR H. HOWELL, M.R.C.P.

WITH old age to-day, the emphasis has been laid on the new geriatric units or departments which, it is hoped, will solve the problem of the aged chronic sick. But every physician and surgeon who is treating elderly patients echoes the same cry: "Why didn't we get these sooner." The geriatric departments of the present resemble an Army base hospital. The damage has been done before the patients get there. All of them have gone down the line, from hospital to hospital, before they come to the place in which serious treatment begins. In many parts of the country there is no special unit which welcomes these patients.

Time and again in general practice and at the Royal Hospital, Chelsea, I saw some relatively trivial illness develop into a major disease when neglected. It is only necessary to compare the incidence of diseases with the cause of death to become aware of this.

Provisional diagnosis
4,622 pensioners

Causes of death
250,000 over 65 (1942)

Bronchitis	14%	Cardiac disease	30%
Senility	12%	Cerebral vascular	14%
Myocardial degeneration, &c. ..	10%	Cancer	12%
Influenza	8%	Bronchitis	7%
Minor surgical	8%	Old age	6%
Dyspepsia	8%		

As for the terms "senility" and "debility", I have kept a record of the ultimate diagnosis of cases with these provisional diagnoses. About a third of these had some cancer, usually in the large gut; another third developed some form of cardiovascular failure; many of the remainder had hidden sepsis, usually in the urinary system. Another group of cases are those who die with a terminal bronchopneumonia. The original disease in these patients may be a true chronic bronchitis, a long-standing arthritis, a fractured femur, or some past cerebral vascular lesion. In the same way, many cases dying with gangrene of the leg have begun with some small injury or infection of the foot. This was neglected at first, then treated too vigorously too late, by putting the patient to bed which altered the state of his circulation and allowed the gangrene to spread.

In old age, prevention is better than cure, as well as being easier. An experienced general practitioner will often ward off serious illness in his old patients time after time, in a way undreamt of by younger men. When I was at the Royal Hospital, Chelsea, I found it possible to reduce the death-rate by admitting pensioners to the infirmary at an early stage of their illness. The patients found in the chronic hospitals are usually those who have been mismanaged in the early stages of their illness. Such conditions as chronic arthritis, hemiplegia and incontinence of urine can be treated successfully in the majority of patients. Most old folk labelled "senility" can be physically rehabilitated to a considerable extent.

If these things can be achieved in a few hospitals which have a geriatric unit, they can be carried on throughout the country. I have treated chronic arthritis and hemiplegic patients successfully in general practice.

A dozen geriatric out-patient clinics in this country would save blocks of hospital beds, and release hundreds of nurses for other work.

The Evolution of a Geriatric Unit from a Public Assistance Institution, 1935-1947

By MARJORY WARREN, M.R.C.S., L.R.C.P.

SINCE 1935—that is during the last twelve years—a geriatric unit has been evolved from a public assistance institution. This unit is now an integral part of the general public health hospital and carries 200 beds. The hospital itself had been appropriated by the local authority (M.C.C.) about five and a half years previously. It is as yet far from ideal, but I venture to suggest that it registers a reasonable step in the right direction.

In June 1935 we took over 874 chronic patients (including 16 maternity and about 144 mental observation patients). I propose to exclude these maternity and mental beds as they are outside the main issue, and in any case other than reducing the number of the mental beds, little has been developed in these wards so far—this left 714 chronic patients, more than half of whom were bedridden, many for long periods of time.

We had the good fortune to be able to transfer, after medical examination, 200 inmates—including elderly and destitute able-bodied workers—to another institution provided for them. This left us with 514.

TABLE V.—DEATHS IN 1947 FOLLOWING ADMISSION BEFORE 10.1.47

Bedfast days	Permanently bedfast	From long-stay annexe	
0- 30 days	M. 0 } W. 0 } 0	M. 4 } W. 5 } 9	
31- 90 days	M. 4 } W. 1 } 5	M. 1 } W. 3 } 4	
91-180 days	M. 1 } W. 2 } 3	M. 3 } W. 0 } 3	
181-365 days	M. 0 } W. 0 } 0	M. 4 } W. 0 } 4	
1- 2 years	M. 4 } W. 3 } 7	M. 0 } W. 0 } 0	
Over 2 years	M. 6 } W. 3 } 9	M. 0 } W. 0 } 0	
Total	24	20	

The third column shows the number of patients with their period of residence in bedfast wards before and after residence in the long-stay annexes, the average being 94 days.

The bedfast cases had diminished from 35 to 19, due to deaths and, in two cases, rehabilitation which had been delayed into the third year of the analysis because our very able physiotherapist, Miss Nunn, could not deal with such a problem alone in a short time. Rehabilitation is now rendered easier by the training of four physiotherapy aides who considerably ease the work of the department. The reduction in the number of occupants of the long-stay annexes from 107 to 81 should be noted, although their places have been filled by the 1947 admissions.

Criticism of the results obtained must be conditioned by the proportion of direct admissions, the length of the waiting-list and the proportion of cases transferred from other hospitals or other hospital departments.

As the period of rehabilitation must depend upon how much previous neglect had ensued before effective treatment commenced, these figures may not be exactly comparable with other geriatric departments. It is essential, however, to ascertain the necessary length of bedfast stay for the elderly patient who has not been adequately treated for more than a period of weeks. We hope this will be a natural consequence of the establishment of geriatric departments. Although the results are not yet completed the twelve months' period of examination ending 31.12.47 more than confirms the earlier results; the advantage of the latter period has been the rehabilitation rate equalling the rate of admission without a large number of bedfast patients awaiting rehabilitation in hospital. In the latter half of 1947 the waiting period before admission had been reduced to a few days.

Table VI shows the time spent in the long-stay annexes by the 20 patients mentioned in Table V, before readmission to the acute geriatric ward where death occurred.

TABLE VI.—DURATION IN LONG-STAY ANNEXE (AVERAGE 1 YEAR 315 DAYS)

0- 90 days	M. 0 } W. 0 } 0	181-365 days	M. 3 } W. 0 } 3	Over 2 years	M. 5 } W. 7 } 12
91-180 days	M. 3 } W. 1 } 4	1-2 years	M. 1 } W. 0 } 1		

Summary.—An analysis was made of 781 admissions over 60 years of age during a recent twenty-six-month period to the Geriatric Wards of Orsett Lodge Hospital in the Essex County Council Social Welfare Department. This showed that of the 296 (38%) deaths, 85% had occurred after less than six months' hospital stay, while 8% (3% of the total admissions) occurred more than twelve months later.

The total number of rehabilitated patients (51% of the admissions) consisted of 284 (37%) who were discharged and 107 (14%) who were in Long-Stay Annexes for the Frail Ambulant, or Ambulant, residents at the end of the twenty-six-month period (10.1.47).

Of the 166 residents on 10.1.47 (21%) the bed patients were found to consist of 35 (4.5%) permanently bedfast (over six months) and 24 (3%) who were receiving active treatment. The long-stay permanently bedfast cases are considered to be 10% of the total admissions.

A further analysis of the 166 residents on 10.1.47, one year later, showed that the permanently bedfast long-stay cases had fallen to 2.5% while the 44 deaths fell into three distinct categories:

- (i) The short-term deaths (8).
- (ii) The long-term deaths after more than twelve months' permanent bedfastness (16).
- (iii) Deaths following a period of residence in the long-stay annexes for ambulant or frail ambulant cases (20).

The average length of stay of discharged patients was found to be 51.6 days and the average length of stay of the patients who died was found to be 87.6 days.

To Dr. Bullough, the County Medical Officer of Health for Essex, to Professor Greenwood, the Consulting Statistician, and to Mr. W. H. Leak, the County Statistical Officer, I express my gratitude for much helpful criticism and advice.

Section of Experimental Medicine and Therapeutics

President—Professor H. P. HIMSWORTH, M.D.

[October 21, 1947]

DISCUSSION ON RENAL CIRCULATION

Dr. Joseph Trueta and Dr. A. E. Barclay [*Summary*]: In March 1941 cases described as "crush syndrome" were recorded. Following severe crushing, usually of the lower limbs, apparent recovery was followed by progressive impairment of renal function and death from renal failure about a week after the injury had been sustained. This clinical picture was soon established as more cases were recorded. Various theories were put forward to account for the sequence of events, none of which seemed to give a satisfactory explanation. Trueta and Barnes, working in Oxford, thought that the explanation might perhaps lie in some reflex effect on the vascular supply of the kidney, causing ischæmia. They therefore produced a condition in rabbits resembling crush injury by the application of a tourniquet to one of the hind-limbs for a period of four and a half hours. It was found after removal of the tourniquet and on injecting radiopaque material into the abdominal aorta that there was active spasm of the femoral artery which might persist for days. The circulation below this zone of spasm was greatly restricted, if not actually suppressed. Further, it was noted that a similar type of spasm frequently occurred in the femoral artery of the uninjured leg and sometimes extended up the internal iliac arteries. Was it possible that a similar type of spasm also affected the renal circulation?

Owing to war conditions, it was not possible to continue the work till September 1945 when a team was formed at the Nuffield Institute for Medical Research, Oxford, to follow up clues given by these early experiments. This team consisted of a surgeon (Dr. Trueta), a physiologist (Dr. Franklin), a radiologist (Dr. Barclay) a pathologist (Dr. Daniel), and a graduate assistant (Miss Prichard).

A technique was devised by which a radiopaque substance, thorotrast, was injected through a cannula into the jugular vein. X-ray cinematograph records, which gave accurate timing of the progress of the opaque blood, were made of the vessels of the kidney as the blood passed through them. From these records on control animals, it was shown that the renal artery was visualized in three seconds and the renal vein in six seconds from the time of injection. The field of the X-ray ciné was, however, of limited size, and it was clear that information as to other vessels was needed. X-ray ciné-recording was therefore replaced by taking single large-size films at the critical times of three and six seconds from the time of the injection. These films included virtually the whole animal. It was found that after the tourniquet had been applied definite changes occurred in certain vessels and, in particular, there was definite narrowing of the renal artery and an increase in the size of the renal vein. It was also noted that sometimes the renal vein was already visible when, according to the control, only the renal arteries should have been seen. This suggested a disturbance in the circuit time of the blood through the kidney. To investigate this the X-ray ciné was used to check the times, and it was found that whereas in the normal animal the circuit time from the renal artery to the renal vein was three seconds, in the tourniquet animals it might be reduced to almost a half of this time. This could only be explained on the hypothesis that the blood had not traversed the whole kidney but had taken a short circuit, so arriving in the renal vein more rapidly.

The next stage was to make direct observations by means of laparotomy on animals that had been subjected to a tourniquet on the leg. In these experiments, the surface of the kidney was often found to be very pale and bloodless. The colour of the blood in the renal vessels was also clearly seen and it was noted that there

At this time, not only was there a greater demand for beds for the elderly (for treatment and for custodial care) but there was also a general desire and need to expand all the hospital services. Both these conditions are likely to happen again this year. As a result everybody cast their eyes to the chronic wards and wanted some of the beds—empty of course, for nobody wanted to take over the chronic sick. But they were full and at that time seemed likely to remain so.

The removal of the 200 patients did not, as might be hoped, leave us with 200 empty beds, for the first move in the plan of betterment was to reduce the bed numbers to correct spacing for treating sick patients. This reduction was undertaken gradually during the next two years so that during the whole transition period we were open to admit new patients.

Between June 1935 and March 1936 every one of the 514 patients was fully examined medically and in many instances socially too. In March 1936 our first big move in classification of patients was undertaken.

Three types of patient were removed from the sick geriatric wards: (1) Up and about patients awaiting discharge to relatives or transfer to resident homes; (2) incontinent patients, (3) cot-bed patients.

During the next three years equipment comparable to that on the acute medical wards and special equipment required on geriatric wards was provided. The wards were painted in light colours and generally brightened up. Swing doors replaced the narrow fixed doors. Lighting was improved.

As a direct result the burden of medical work and nursing care was lightened, and gradually a number of very long-stay inmates were improved satisfactorily and in time discharged to their homes.

As an indirect result in 1939 one ward of 45 patients was emptied and handed over to the T.B. Service and it has remained ever since in use for female T.B. patients. One ward of 22 beds was handed over to the skin department and one ward of 18 beds was converted into: (a) Small gymnasium. (b) Second X-ray department.

Progress continued in spite of the difficulties and frustration of war and in the absence of further major improvements. With the quicker turnover of patients, further wards were given to other departments to help in the overall expansion of the hospital.

And so to date I have a compact geriatric unit of 200 beds, and two full-time house physicians appointed. Recently I have been asked to undertake in addition the medical supervision of the 200 patients in the Resident Home (P.A.I.).

We are therefore caring for 200 hospital elderly sick and 200 institutional elderly persons in 400 beds instead of 714 chronic sick and destitute mixed up in wards which required a 24-hour nursing service and gave no opportunity for adequate care or teaching.

Dr. E. L. Sturdee: The three speakers have shown, in their own hospitals, that patients thought to be bedridden can be put on their feet again. Many of the results they are achieving would seem like miracles to the medical staffs of hospitals where similar methods have not been tried.

It looks as though two lines of research are needed. Professor J. B. Duguid, speaking recently at the Professional Nurses and Midwives Conference, stated that old age did not kill, but that there was always some pathological cause of death. Research is needed, therefore, into the difference between the pathological or preventable processes of old age and those that are natural and inevitable.

The second and more easily managed research is into the early symptoms of chronic diseases, and into the methods of preventing their crippling results. This requires a knowledge of clinical medicine in elderly persons, and the availability of specialist consultant advice for the family doctor. Some alteration, therefore, is necessary in the training of doctors and nurses, because at present they learn little, as students, of the diseases which will form a large part of their future practice.

Speaking generally, the teaching hospitals have no room to set up a new department of medicine in their buildings, but the municipal hospitals have the wards to spare, and the patients. The latter hospitals will soon become the property of the Regional Hospital Boards, and careful thought will be required to decide the best methods of co-operation between the teaching hospitals and the Boards, so as to ensure that the problem of the chronic sick is given the attention it deserves.

CORRECTION

Section of Epidemiology and State Medicine, *Proceedings of the Royal Society of Medicine*, 41, 165, March 1948.

The final sentence of Sir John Taylor's paper on "Epidemiology of Cholera", p. 176, line 2, should read: "The possession of an inoculation certificate does not of course ensure complete freedom from risk."

Section of Experimental Medicine and Therapeutics

President—Professor H. P. HINSWORTH, M.D.

[October 21, 1947]

DISCUSSION ON RENAL CIRCULATION

Dr. Joseph Trueta and Dr. A. E. Barclay [Summary]: In March 1941 cases described as "crush syndrome" were recorded. Following severe crushing, usually of the lower limbs, apparent recovery was followed by progressive impairment of renal function and death from renal failure about a week after the injury had been sustained. This clinical picture was soon established as more cases were recorded. Various theories were put forward to account for the sequence of events, none of which seemed to give a satisfactory explanation. Trueta and Barnes, working in Oxford, thought that the explanation might perhaps lie in some reflex effect on the vascular supply of the kidney, causing ischæmia. They therefore produced a condition in rabbits resembling crush injury by the application of a tourniquet to one of the hind-limbs for a period of four and a half hours. It was found after removal of the tourniquet and on injecting radiopaque material into the abdominal aorta that there was active spasm of the femoral artery which might persist for days. The circulation below this zone of spasm was greatly restricted, if not actually suppressed. Further, it was noted that a similar type of spasm frequently occurred in the femoral artery of the uninjured leg and sometimes extended up the internal iliac arteries. Was it possible that a similar type of spasm also affected the renal circulation?

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A technique was devised by which a radiopaque substance, thorotrast, was injected through a cannula into the jugular vein. X-ray cinematograph records, which gave accurate timing of the progress of the opaque blood, were made of the vessels of the kidney as the blood passed through them. From these records on control animals, it was shown that the renal artery was visualized in three seconds and the renal vein in six seconds from the time of injection. The field of the X-ray ciné was, however, of limited size, and it was clear that information as to other vessels was needed. X-ray ciné-recording was therefore replaced by taking single large-size films at the critical times of three and six seconds from the time of the injection. These films included virtually the whole animal. It was found that after the tourniquet had been applied definite changes occurred in certain vessels and, in particular, there was definite narrowing of the renal artery and an increase in the size of the renal vein. It was also noted that sometimes the renal vein was already visible when, according to the control, only the renal arteries should have been seen. This suggested a disturbance in the circuit time of the blood through the kidney. To investigate this the X-ray ciné was used to check the times, and it was found that whereas in the normal animal the circuit time from the renal artery to the renal vein was three seconds, in the tourniquet animals it might be reduced to almost a half of this time. This could only be explained on the hypothesis that the blood had not traversed the whole kidney but had taken a short circuit, so arriving in the renal vein more rapidly.

The next stage was to make direct observations by means of laparotomy on animals that had been subjected to a tourniquet on the leg. In these experiments, the surface of the kidney was often found to be very pale and bloodless. The colour of the blood in the renal vessels was also clearly seen and it was noted that there

were frequently streams of bright arterial blood flowing with the dark blood in the renal vein. Moreover, on several occasions the *whole* of the blood seen in the renal vein was as red as in an artery. Even more striking was the fact that this vein, apparently filled with arterial blood, occasionally exhibited pulsation that was almost comparable to that in an artery. It seemed obvious from this series of observations that these phenomena could only be explained by the presence of anastomotic channels in the kidney through which the blood was short-circuited in response to the stimulus produced by the application of the tourniquet.

The next step was the injection of dyes or Indian ink, either direct into the renal artery or via the aorta. In the control, the coloured blood was at once seen to perfuse the surface of the kidney and to pass out through the renal vein; but in the tourniquet animals, although the coloured blood passed out by the renal vein, the surface of the kidney was unaffected, i.e. although the coloured blood had traversed the kidney it had failed to pass to the surface of the cortex. When these kidneys were cut in half the staining of the dye showed that in the tourniquet animal the blood had short-circuited within the kidney and that virtually none of it had reached the surface of the organ or the glomeruli in its cortex.

The short-circuit was evidently of such dimensions that it suggested an anastomotic communication that ought to be anatomically demonstrable, yet stereoscopic radiographs of injected kidneys failed to show any trace of such connexions. The short-circuit must therefore lie in vessels too small to be seen with the naked eye. It was then found by histological investigation and radiography that the main channels of short-circuit lay about the internal area of the cortex, filling the vasa recta of the medulla of the kidney. These vessels are multitudinous and are considerably larger than capillaries. They appear to be the main channels that provide this alternative route for the blood flow. Many of them arise from the larger glomeruli which Heggie has named juxtamedullary glomeruli. The suggestion is that this, and perhaps other alternative paths of flow, are an anatomical physiological feature of the vascular supply of the kidney. They are under direct or indirect control of the nervous system, for, after cutting the splanchnic nerve, the application of a tourniquet failed to produce any appreciable effect on the renal circulation. It seems clear, therefore, that in the "crush syndrome" the persistent nervous stimulation causes a short-circuit of blood away from the cortex of the kidney; and if the consequent ischæmia persists long enough, impairment of function and even necrosis will result.

It is suggested that in cases of vascular hypertension, the cortex of the kidney tends to be short-circuited and out of action too frequently. Nature's response is to raise the blood-pressure, thus opening up the cortex and bringing the glomeruli into function. If this is successful, the patient remains well, apart from the raised blood-pressure that is necessary to keep the cortex of the kidney in function, and the kidneys remain normal. It is only when the blood-pressure fails to open up the renal cortex that symptoms of uræmia develop and pathological changes occur in the kidney.

Dr. J. F. Heggie: When the rate of renal blood flow is measured directly in the normal anæsthetized rabbit by the method of Dunn, Kay and Sheehan (1931) it is found to lie between 2 and 4 c.c. per gramme of kidney substance per minute, commonly between 2.5 and 3 c.c. per gramme per minute.

When finely particulate carbon ("Hydrokollag") suspended in serum is injected into the renal artery in the normal anæsthetized rabbit, at the same rate as the blood flow therein, for two to three seconds and the pedicle immediately clipped the renal vascular architecture is clearly demonstrated and the pigment is found in the inter- and intralobular arteries, the afferent glomerular arterioles and glomeruli, and the essentially glomerular character of the circulation as described by Bowman (1842) is demonstrated. The efferent glomerular arterioles in the cortex are usually smaller

than the afferent vessels and are relatively short, they soon break up to join in the peritubular capillary plexuses. The efferent vessels of the glomeruli situated near the medulla, to which in 1941 I gave the name *juxtamedullary glomeruli*, provide the blood supply to the medulla; these vessels are large, larger than the corresponding afferent vessels, and long, and run a fair length before they break up to form very rich capillary arcades and networks around the tubules in the pyramid, the loops of Henle and the collecting tubules. A similar architecture obtains in the human kidney.

Microdissection of the glomerulus shows the afferent vessel to branch after the manner of an artery into subdivisions which give rise to capillaries; in like manner the venous capillaries unite and the efferent arteriole is formed. This point, which is not generally appreciated, is well illustrated in Bowman's paper (1842) and in Vimtrup's semidiagrammatic representation (1928).

The volumes of representative glomeruli in the rabbit kidney in the usual normal state of the circulation and in acute toxic glomerulitis in which there is extreme dilatation of all glomerular capillary loops, were obtained from measurements made on enlarged serial photomicrographs (at 2,000 diameters). The number of glomeruli per kidney was ascertained from partial and total counts—and found to be around 200,000. The glomerular capillary rate (velocity) was then computed to be 1.25 mm./sec.—when it was assumed that all the glomeruli were functioning (as there is good reason to believe is the case in the healthy mammal) and provided they were operating equally. The glomerular volume was calculated to be changed five times each second. These velocity and other values are not altogether unexpected having regard to the fact that the glomerular capillaries are interposed between arterioles and the pressure in them is very high.

In experimental renal cortical necrosis changes in the circulation within the kidney occur from the outset and Dr. Trueta and his colleagues (1947) have described blanching of the kidney cortex within two minutes of the injection of a large dose of staphylococcus toxin and the appearance of rapid red pulsatile streams in the renal vein from the seventh minute, maximal at fifteen minutes and continuing until the death of the animal five minutes later. In such acute experiments, if the minute volume of the renal blood flow remains the same and if the intrarenal pathway is via normal-sized *juxtamedullary glomeruli* alone, the glomerular volume of these is changed almost thirty times each second and the velocity is proportionately increased; but if the *juxtamedullary glomerular capillaries* are dilated (and they can so accommodate the entire normal glomerular capillary volume of blood) the rate of change of their augmented volume is five times per second and the velocity in the dilated capillaries is still at the normal rate of 1.25 mm./sec.

But in the slightly less acute experiment of this kind with which I am more familiar there appears to be practically no immediate phase of vascular contraction or medullary diversion, the initial lesion is one of general glomerular capillary dilatation, an inflammatory reaction in the true sense, which after initial hyperæmia shows gradual slowing so that between the second and third hour there is diapedesis of red blood cells and stasis in the cortex while the circulation in the medulla continues through the much-dilated *juxtamedullary glomeruli* and their ample efferents. In these animals the total renal blood flow is just below normal. Resolution occurs in a few animals which recover after a period of oliguria but in many the cortex becomes necrotic while the medulla, not so affected, by contrast enjoys a blood flow, via the *juxtamedullary glomeruli* which is increased fivefold and is changed at almost the normal rate of five times each second, or slightly less. It was with a knowledge of these changes, which I had demonstrated to the Pathological Society of Great Britain in 1941, that following the preliminary communication of Dr. Trueta and his colleagues (1946) I suggested in a letter to the *Lancet* (1946) that the diversion of the

circulation to the medulla, which they had demonstrated, was effected via the juxtamedullary glomeruli.

But these changes are the one extreme of a wide range; at the other are variations of the normal. Changes occur with the diminished blood flow of hypotension and shock which follow major hæmorrhagic accidents, and, in pregnancy, fatal anuria and cortical necrosis sometimes follow concealed accidental hæmorrhage.

Less severe hæmorrhagic accidents with marked oliguria and disturbance of filtration and tubular function (as after abortion) may be followed by recovery (Humphrey *et al.*, 1947) and important disturbances of the renal circulation occur also in the crush syndrome and other conditions, but it is not proposed to discuss at present the consequent variations of filtration and reabsorption rates, water metabolism, and electrolyte and urea retention.

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Dr. E. M. Darmady said that cortical necrosis following severe accident was not very common. There were, however, certain features found histologically in such cases which did fit in very well with the findings shown at the meeting. The bloodless glomeruli, the tubular venous rupture at the juxtglomerular area, and the congestion of the parts of the medullary zone were among these. He felt that it was not quite fair to compare the findings in the rabbit with the human at this stage, because one knew that experimentally it was easy to induce an ischæmia by traction on the kidney. They should be guarded before arguing from the rabbit to man.

Mr. R. H. Paramore said that little had been heard of the effect of the renal secretion on the renal circulation. Brodie (1914, *Proc. Roy. Soc.*, Ser. B., 87, 571) had stated that when the kidney is in diuresis, due to a saline injection, if one clamps the ureter, the kidney becomes almost bloodless. This fundamental observation throws light on the state of the kidney in eclampsia and in concealed accidental hæmorrhage. It is very important to observe that the association of anuria with accidental hæmorrhage only occurs when the blood, poured out into the uterus, is concealed: when the blood can freely escape by the vagina, anuria (symmetrical cortical necrosis) does not occur. Owing to the shape and structure of the kidney, when the pressure in the cortex rises (relaxation of arterioles), medullary parts are thrust towards and into the renal pelvis—just as when the pressure in the renal pelvis becomes raised (ureteric obstruction) the medullary parts of the kidney are thrust and compressed against the cortex.

The President (Professor H. P. Himsworth) said that he had been interested in the hepatic circulation and had found that in carbon tetrachloride poisoning and dietetic necrosis of the liver in rats rearrangements of the circulation occurred, not as primary phenomena, but as secondary effects due to swelling of the hepatic parenchyma compressing the sinusoids and so producing ischæmia. The relevance of these observations to the present discussion was that the same measures which produced dietetic hepatic necrosis produced necrosis of the renal cortex in younger rats and Dr. Hartroft, working in Professor Best's laboratory in Toronto, had shown that the ischæmia of the renal cortex, which was such an important factor in completing this type of necrosis, was, not a primary phenomenon, but secondary to a swelling of the renal parenchyma which compressed the cortical blood-vessels. Clearly such swelling would produce the rearrangement of the intrarenal circulation demonstrated by Drs. Trueta and Barclay, namely exclusion of blood from the cortex and its diversion through the juxtamedullary glomeruli to the medulla. While not denying that reflex nervous mechanisms might also cause such a rearrangement it was important to keep in mind the possibility that purely mechanical factors, such as parenchymal swelling, might also be of importance—perhaps more importance—in the pathogenesis of fully-developed cortical necroses.

CORRECTION

Section of Experimental Medicine, *Proceedings*, Vol. 41, pp. 221 and 222, Tables I, II and III. The references under Tables II and III, as follows:

Table II from data of Armstrong, Budka *et al.* [2]

Table III from data of Svensson [20]

should be transferred to Table I. These refer respectively to the second and third sections of Table I. The first section of Table I is from data of Perlmann and Kaufmann [17].

Section of Endocrinology

President—L. R. BROSTER, O.B.E., M.Ch.

[February 25, 1948]

Growth and Physical Performance of Children in Relation to Maturity

By RICHARD W. B. ELLIS, M.D.

At the present time the nutrition of the adolescent is the subject of official concern. Boys and girls in the teen-ages are being subjected to assessment on the basis of height, weight and physical performance, with a view to determining whether their growth and nutritional status are satisfactory. For the most part, the mean figures obtained for groups in the same year of age are being used for comparison with similar age-groups either before the present rationing or in different social environments, and for comparing growth of particular groups over a known period.

This assessment of growth and nutrition purely in relation to chronological age is open to certain avoidable errors, and it is the purpose of the present communication to stress the importance of grading on a maturity basis in addition to age when dealing with children from 9 years onward. This also relates more or less directly to the assessment of exogenous obesity in childhood, since some increase of fat deposition is commonly observed at or about puberty in both sexes. Thus a weight increment of 25 lb. in one year may be physiological in a particular boy of 15 at one stage of maturity and pathological in another of the same age in whom evidence of sexual maturation has not begun to appear. Although many studies on these lines have already been made, particularly in America (e.g. Baldwin, 1921; Crampton, 1908; Greulich *et al.*, 1942; Simmons, 1944), it is insufficiently realized that composite growth-curves constructed for children aged 9 to 18 will tend to smooth out the characteristic growth pattern associated with puberty, since the age-onset of puberty shows a wide physiological variation (Ellis, 1947).

An attempt has been made to define three stages of maturity on a purely clinical basis, which would make possible an approximate grading in school or industrial medical examinations. The criteria suggested are as follows:

TABLE I.—MATURITY GRADINGS

	Girls	Boys
Non-pubescent . .	Absence of breast development, pubic hair or menstruation	Absence of pigmented pubic hair; genital development infantile or minimal
Pubescent ..	Early breast development and/or pubic hair; absence of menstruation	Early genital development and/or pubic or axillary hair
Adolescent ..	Menstruation, breast development, and presence of body hair	Development of corpora cavernosa plus advanced enlargement of testis in relation to epididymis plus pubic (and axillary) hair

These criteria are obviously inadequate to serve as more than an approximate index of three stages of maturity but I hope to show that they are considerably better than none. In the case of girls, menstruation could usually be related much more accurately to ovulation if facilities were available for estimation of pregnandiol in the urine, but this is impracticable where large groups are under review. Similarly, it might be possible to subdivide "adolescence" into early or late on a clinical basis, depending on whether a regular menstrual cycle had been established and whether axillary hair was present.

In the case of boys, the absence of a well-defined stigma such as menstruation makes classification more difficult, and border-line cases will inevitably occur. Thus the appearance of pigmented pubic hair is preceded by non-pigmented vellus, and the assessment of the stage of genital development is to some extent arbitrary. In general, growth in length of the penis precedes adolescent development of the corpora cavernosa, whilst a pubescent stage of testicular development can usually be distinguished in which the body of the testis is enlarged in relation to the epididymis, is softer than in the prepubescent state, but is less than half the adult size. Penile development may precede testicular development or vice versa. For the grading of adolescence, well-marked development both of penis and of testicles is necessary, in association with pubic hair; the appearance of axillary hair is too variable to serve except as a confirmatory sign, since in some cases it was found to appear very late and occasionally in advance of pubic hair and before genital development was apparent; hair on the linea alba was only observed when adolescence was well advanced. The pitch of the voice is also regarded as confirmation of adolescence when the voice is obviously "broken", but the pitch cannot be estimated on a single examination with sufficient accuracy to be of much clinical value.

In a series of 208 boys aged 11 to 16 to whom these gradings were applied, it was found that gynæcomastia was present in none of the non-pubescent boys, in 12.9% of the pubescent, and in 32.1% of the adolescent. It bore no obvious relationship to

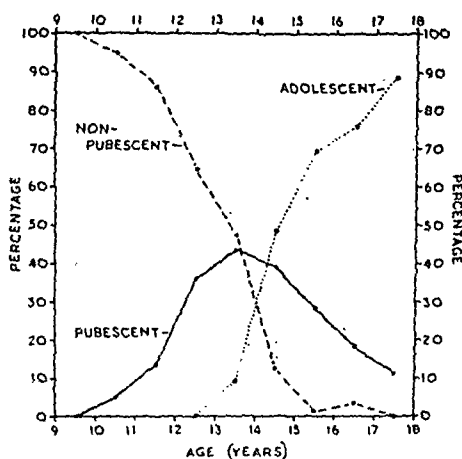


FIG. 1.—Percentage of boys non-pubescent, pubescent and adolescent in each year of age (9 to 18).

the presence or absence of axillary hair. Comedones were noted in 19.7% of the non-pubescent, 41% of the pubescent, and 76.2% of the adolescent boys (Ellis, 1946).

On the basis of 662 examinations, the percentage of boys graded as non-pubescent, pubescent, and adolescent in each year of age between 9 and 18 was as shown in fig. 1.

This illustrates the effect which the raising of the school-leaving age from 14 to 15

will have on the maturity of boys entering employment. Whilst at 14 the percentage of completely immature boys is greater than the percentage graded as adolescent, at 15 the percentage of "non-pubescent" boys is less than 10 and that of adolescents approximately 60. The distribution curve of pubescent boys shows a peak between 13 and 14 years (at which age the division into non-pubescent and pubescent is most even).

If the same data are replotted (fig. 2) to show the percentage of boys non-pubescent and the percentage non-adolescent in each year of age, the curves suggest that the duration of pubescence is longer in those maturing early or late than in those maturing at the mean age (Ellis, 1948).

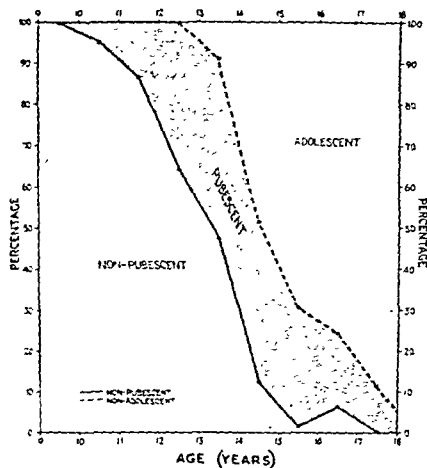


FIG. 2.—Percentage of boys non-pubescent and non-adolescent in each year of age (9 to 18), to show duration of pubescence.

Height and Weight.—Using the maturity-grading described, an initial comparison was made of the mean height and mean weight of boys of the same year of age but of different degrees of maturity, with the result that within the age ranges studied, viz. 12 to 16 years, the groups of more mature boys were found in every instance to be heavier and taller than the groups of less mature boys of the same year of age. These boys were all resident in two schools (referred to as Schools A and B) and since comparisons were only made between boys in the same school, each group had been living under similar environment and on the same school diet as the group with which comparison was made for periods of from 3 to 10 years.

The differences in each instance between the mean heights and weights of boys of similar age but in different maturity groups were statistically significant (Ellis, 1946).

In order to determine at how early an age these differences were apparent, mean height and weight curves were constructed for each maturity-age group, and those for boys of the same age and school compared. It was found that whilst the curves tended to diverge with increasing maturity, the groups of earlier-maturing boys were in all instances heavier and taller than their later-maturing contemporaries to the earliest age for which measurements were available, i.e. in the case of School A, the sixth year of age. Whilst it cannot be argued from this that a small child will necessarily mature late or a large child early, it is of interest that differences in the average heights and weights of different maturity groups were manifest long before changes directly attributable to onset of puberty had occurred.

In order to determine more accurately the rate of growth associated with each phase of maturity, 154 of the boys examined in the two residential schools were

subsequently regraded (a year later in the case of School A, and nine months later in the case of School B), and their increase in height and weight estimated a year after the initial grading. They were grouped into those who had remained non-pubescent throughout, those who were non-pubescent on first and pubescent on second grading, those who remained pubescent throughout, those pubescent on first and adolescent on second grading, and those adolescent throughout. The age-ranges at the end of the experimental period were 12 to 13 and 13 to 15 in School A and 14 to 16½ in School B (Ellis, 1948).

Fig. 3 shows the results in the case of School B. There were no boys who remained non-pubescent throughout the experimental period 1946-7, but the rate of "non-puberty" growth is indicated by Group I in 1945-6. Whilst the differences between

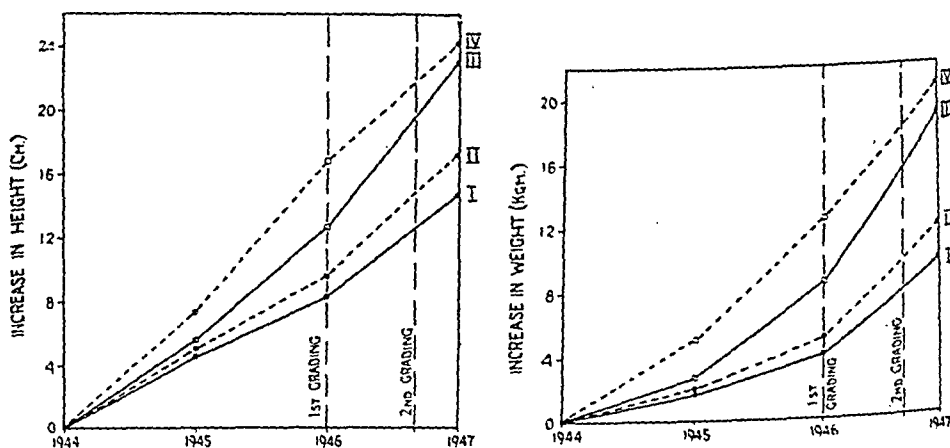


FIG. 3.—Mean annual height and weight increments over a three-year period of boys aged 14 to 16½ in 1947. Group I non-pubescent on first and pubescent on second grading; Group II pubescent on first and second grading; Group III pubescent on first and adolescent on second grading; Group IV adolescent on first and second grading.

(FIGS. 2 and 3 are reproduced from *Arch. Dis. Childh.*, 1948, 23, pp. 20 and 25.)

the height and weight increments of Groups I and II (who were both pubescent on second examination), were not statistically significant, it is seen that the passage from pubescence to adolescence (Group III) is associated with a rapid acceleration in both height and weight gain. In Group IV, who were adolescent on first examination, the rapid weight gain seen in 1945-46 is continued throughout the experimental period, but gain in height is beginning to be retarded.

The findings in both schools showed an acceleration of both height and weight increment preceding the clinical manifestations of pubescence, and continuing through the period of pubescence; and a more rapid gain in both height and weight associated with attainment of adolescence, and continuing into early adolescence. The boys who passed from pubescence to adolescence, and those who were adolescent on both examinations, showed an increase in height which is nearly double and an increase in weight which is more than double that of the boys who remained non-pubescent over a twelve-month period.

Hip circumference.—It was noted clinically in the course of the examinations that the onset of puberty was in many cases associated with some degree of fat-deposition in the pelvic region and with muscular development, particularly of the buttocks. It was therefore decided to measure the circumference of the hips at the level of the great trochanter in order to see whether this bore any correlation to the degree of maturity. The pooled results in this instance are given for 267 boys aged 12 to 17

examined in 1947 from the four institutions, and are divided first into maturity groups and secondly into year-age groups.

TABLE II.—HIP-CIRCUMFERENCE RELATED TO MATURITY AND AGE

Maturity	Mean age		No.	Mean circumference (cm.)	Standard deviation	Standard error
	Years	Days				
1. Non-pubescent	12	172	35	70.34	3.20	0.54
	13	141	36	72.17	3.51	0.59
	14	216	9	73.22	2.35	0.78
2. Pubescent	12	232	19	75.37	2.41	0.55
	13	170	22	76.11	3.88	0.83
	14	163	32	76.82	3.92	0.70
	15	153	15	76.13	4.01	1.04
	16	151	8	75.08	3.22	1.36
3. Adolescent	13	234	4	81.38	4.26	2.13
	14	208	30	84.18	4.07	0.74
	15	172	32	85.36	3.98	0.71
	16	168	25	84.29	3.71	0.76

It will be seen that the mean measurements are related more closely to the state of maturity than to chronological age. Thus the means for the pubescent boys at each age are greater than those of the non-pubescent, and those of the adolescents again greater than those of the pubescent boys, irrespective of age. Amongst the boys graded as pubescent (the most homogeneous of the maturity groups), the means are closely similar, whether the boys are aged 12, 13, 14, 15, or 16 years. The differences between the means of the 12 and 15 year-old pubescent boys are not statistically significant.

Whilst there can be only limited value in a measurement which involves at least three variables (bone, muscular tissue, and fat), it is suggested that the circumference of the hips might usefully be included in the routine measurements of prepubertal and adolescent boys.

Physical performance.—Using the same groups as shown in Table II, a preliminary investigation of physical performance in relation to maturity and age was made on the basis of dynamometer readings obtained with grip and pull. The same instrument was used in each case, and the tests carried out as far as possible under standard conditions. The test of pull, however, was the less satisfactory of the two, as the range of readings was relatively small and the pull, being performed with flexed thumbs across the chest at nipple level, caused some discomfort when maximum force was exerted.

The results of the dynamometer tests, arranged as in Table II, were as follows:

TABLE III.—DYNAMOMETER READINGS (GRIP AND PULL) RELATED TO MATURITY AND AGE

Maturity	Age-group (years)	No.	Grip			Pull		
			Mean	Standard deviation	Standard error	Mean	Standard deviation	Standard error
Non-pubescent	12-13	35	69.29	11.93	2.02	22.20	5.64	0.95
	13-14	36	75.17	10.87	1.81	23.72	5.04	0.84
	14-15	9	71.33	11.66	3.89	23.33	3.40	1.17
Pubescent	12-13	19	85.63	12.53	2.87	25.00	3.88	0.89
	13-14	22	74.18	9.57	2.04	24.86	4.76	1.01
	14-15	32	83.47	12.22	2.16	25.91	4.89	0.86
	15-16	15	84.87	11.28	2.91	29.27	6.48	1.67
	16-17	8	79.50	4.21	1.49	24.75	4.63	1.63
Adolescent	13-14	4	87.50	16.01	8.00	30.50	5.32	2.66
	14-15	30	109.47	17.23	3.15	31.07	5.60	1.02
	15-16	32	116.59	19.72	3.49	31.94	5.04	0.89
	16-17	25	125.79	21.10	4.31	34.88	4.67	0.95

With the single exception of the 13-year-old pubescent boys, whose mean grip is less than that of the non-pubescent group of the same age, it is seen that these performance tests increase with maturity rather than age. Thus, with the one exception noted, all the pubescent groups give on the average higher readings than all the non-pubescent, and the adolescent groups higher than all the pubescent groups. The performance of the adolescents increases with increasing age; this is consistent with the general findings, since it is to be expected that the older adolescents will on the average be more mature than the younger ones.

Conclusion.—In assessing growth and nutrition of children between 9 and 18, maturity is almost as important as is chronological age. No composite growth curves can form a satisfactory standard of comparison for the individual case unless the curves are constructed from measurements made on children maturing at approximately the same age. The differences in mean rate of growth (as indicated by increment in height and weight over a twelve-month period) have been shown to be in the order of 100% in boys within limited age-ranges and on the same school diet but at different stages of maturity. It is suggested that if a simple form of clinical maturity grading were introduced into routine medical examination of children and adolescents in this country, it would be possible to collect data and construct standards on the basis of height, weight, age and maturity which would be of much greater value than those commonly employed. There are obvious objections to using standards prepared in a different country with different dietetic habits, climate, and social standards. It would also make it possible to determine whether the age-onset of puberty is significantly affected by nutrition, latitude, and social environment as well as by the genetic factors which can be assumed to operate. More information is required with regard to the physiological deposition of fat at puberty, and the distinction between this and pathological obesity. It is unlikely that any mathematical formula relating to height, weight, and physical performance will provide a completely satisfactory answer as to what is within physiological limits and what is not, although many such formulæ have been constructed. But these measurements, if related to both age and maturity, will have a certain value in assessing the nutrition and growth of large groups of children. It is suggested that circumference of the hips might provisionally be added to the measurements made on routine examination of children and adolescents, since this appears to bear a much closer relationship to maturity than it does to chronological age.

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JOINT DISCUSSION No. 1

Section of Endocrinology and Section of Pædiatrics

Chairman—L. R. BROSTER, O.B.E., M.Ch.
(President of the Section of Endocrinology)

[March 24, 1948]

Two Brothers with Infantilism, Showing Some Features of Progeria, associated with Microcephaly, Retinal Degeneration and Intracranial Calcification.—CATHERINE A. NEILL, M.D., and M. M. DINGWALL (for HELEN M. M. MACKAY, F.R.C.P.).

I.—A. P., aged 15. Birth-weight $7\frac{1}{2}$ lb. Seemed normal until about 1 year. Walked at about $2\frac{1}{2}$ years. Cut first tooth at ? over 1 year.

II.—J. P., aged 9 years 11 months. Birth-weight 8 lb. Walked at $2\frac{1}{2}$ years. Tremor since 4 years. First tooth at over 1 year.

Both are attending a school for mentally defective children.

Family history.—Parents normal. Mother's stepbrother reported to be mentally defective but can earn a living. No consanguinity of parents; no history of dwarfism. The patients are two of four siblings: (1) A. P. (2) Male (born 17.4.34) normal. (3) J. P. (4) Female (born 12.7.40) normal.

On examination.—A. P. Very small stature, extremities relatively large. Lumbar lordosis, slightly protuberant abdomen, pes valgus, slight fixed flexion knees, gait "tottering". Pigmented moles numerous on head, neck, arms and legs. Microcephalic but no sloping of forehead; ears prominent, eyeballs sunken. Skin of face stretched, some wrinkling, elsewhere normal, rather rough on hands and feet. Hair dry and thin. C.V.S. normal (apart from retinal vascular changes). B.P. 115/60. R.S. normal. Teeth irregular, grossly carious. Gums hypertrophied. Liver enlarged $1\frac{1}{2}$ fingerbreadths. Spleen enlarged 2 fingerbreadths. Bilateral undescended testes. No secondary sex characteristics. C.N.S.: Pupils slightly irregular, very small, react very slightly to light and accommodation, very low response to mydriatics. Jerks brisk. Plantars flexor. Fundi "degenerative retinitis of the pepper-and-salt type. Optic atrophy both eyes". (Mr. Minton.)

J. P. Very similar. Spleen only just palpable. Liver enlarged 1 fingerbreadth. Blood-pressure 112/60. Teeth less carious; optic atrophy less marked but retinae similar.

Measurements	A. P.	J. P.	Normal brother, 13 years
Weight	30 lb. 5 oz.	34 lb. 14 oz.	
Height	40½ in.	44 in.	57 in.
Upper (crown-symphysis)	18 in.	19½ in.	
Lower (symphysis-sole) ..	21½ in. (R. & L.)	22½ in. (R. & L.)	28½ in.
Ratio (upper : lower) ..	0.85	0.87	
Head circumference ..	18 in.	19½ in.	
Span	38½ in.	42½ in.	59 in.

Investigations:

	A. P.	J. P.
Hb	92%	96%
R.B.C.	4.75 million	5.0 million
W.B.C.	8,400	12,000

P. 54%, E. 2%, L. 42%, M. 2% P. 61%, E. 3%, L. 32%, M. 4%

W.R., Kahn and jelly (tuberculin) tests all negative.

	A. P.	J. P.
Serum potassium ..	22.2 mg. %	21.4 mg. %
Serum phosphate ..	3.37 mg. %	3.71 mg. %
Serum phosphatase ..	17.4 units	15.3 units
Serum calcium ..	10.0 mg. %	9.9 mg. %
Serum cholesterol ..	195 mg. %	240 mg. %
Serum protein ..	6.92 (A. 4.99, G. 1.93)	6.10 (A. 4.86, G. 1.24)
Serum chlorides ..	600 mg. %	588 mg. %
Serum sodium ..	344 mg. %	344 mg. %
Blood urea ..	38 mg. %	44 mg. %
Urea clearance ..	83% of normal	78% of normal
Thymol turbidity ..	4 units	4 units
Non-protein nitrogen	41 mg. %	50 mg. %
Urine:	Normal	Normal
Urinary amino-acid nitrogen	44 mg./100 c.c. (both within normal limits)	94 mg./100 c.c.
Urinary 17-ketosteroids (by Dr. Patterson)	2.0 mg./24 hr. (both low values)	1.1 mg./24 hr.
Sugar tolerance (1½ grammes/kilo):	Urine	Urine
Fasting	70 mg. %	84 mg. %
½ hour	200 mg. %	204 mg. %
1 hour	195 mg. %	191 mg. %
1½ hours	79 mg. %	66 mg. %
2 hours	43 mg. %	52 mg. %
B.M.R. (Dr. E. C. Pillman-Williams) — 17.5% (calc. on weight or on age)	Sugar plus	Sugar plus
		— 47.5% (unsatisfactory test)

X-rays: Skull shows intracranial calcification, probably choroid plexus. Long bones show slight generalized osteoporosis.

Mental state (Miss M. M. Dingwall).—Tests used: Merrill Palmer, Revised Stanford Binet Form L, Gesell's norms. A. P.: Chron. age 14 years 10 months. Mental age 2 years 4 months. J. P.: Chron. age 9 years 9 months. Mental age 2 years 5 months.

Although both these children are idiot one establishes a very good contact with them, and their reactions are much quicker than one would expect from this level of intelligence.

The lively emotions and the fact that the hand movements are almost adult are among the more interesting psychological observations.

[It is hoped to publish a fuller account of these two patients in the *Arch. Dis. Childh.*]

Dr. Leo Rau agreed that these two brothers were examples of a very rare condition. He had never seen anything similar in children. The main signs were the low B.M.R.; the splenomegaly; the marked hypoglycaemia; the retinal abiotrophy; and the mental changes. A similar case was shown by him at the Clinical Section on March 14, 1947 (*Proc. R. Soc. Med.*, 40, 468). This patient had in addition to the changes mentioned inner-ear deafness, and an abnormally slow water clearance. The treatment in this case was thyroid by mouth, which led to a complete disappearance of symptoms and signs.

Three Cases of Precocious Puberty.—N. F. ELLIOTT BURROWS, B.M. (for W. G. WYLLIE, M.D.).

I.—S. T., aged 7½ years.

History.—Normal baby till 1 month of age when mother noticed a white discharge from her vagina. This continued periodically. At 2 months of age she had pubic hair and her breasts were developed but she did not have any teeth until 11 months of age.

Although at 6 months a pinkish-red stain was noticed on her napkins on two occasions she did not start menstruating properly until 1 year and 7 months since when her periods have been fairly regular.

Family history.—Normal. One other sib. alive and well.

Investigations.—17-ketosteroids 2.8 mg. per day. X-ray of skull normal. Wrist X-ray showed bone age of about 12 years.

On laparotomy an enlarged uterus similar to that of a girl of 16 was found. Her left ovary contained a corpus luteum and a maturing follicle. Ventriculography showed normal filling of the ventricles. She is now 7½ years of age and becoming increasingly difficult to manage.

II.—Y. G., aged 6 years.

History.—Breasts started to enlarge soon after birth and her external genitalia developed rapidly with her age but her first menstrual period was at 4 years of age.

Family history.—Normal.

Investigations.—17-ketosteroids varied between 2.2 and 2.4 mg. per day. Ventriculography showed normal ventricular system. X-ray of skull normal. X-ray of wrists showed bone age of about 13 years. W.R. positive.

In November 1945 laparotomy was performed and a uterus corresponding to that of a girl of 16 and large cystic ovaries were found; $\frac{2}{3}$ of each ovary was removed. The left suprarenal gland seemed larger than normal. She is now very well developed with adult breasts and some axillary and pubic hair, and is menstruating regularly. Her W.R. remains positive in spite of large doses of penicillin and arsenic.

III.—D. A., aged 2 $\frac{1}{2}$ years.

History.—At the age of 3 months her "mother" noticed a white discharge from her vagina. At 6 months hair was noticed in her pubic region. At 8 months she seemed to be getting over-weight and it was noticed that her breasts were enlarging.

Family history.—Adopted child; nothing known of parents.

Investigations.—17-ketosteroids 0.5 mg. per day. Laparotomy revealed a large uterus similar to that of a girl of 16 years and also enlarged ovaries—the left being firm and the right obviously cystic. X-ray skull normal, X-ray wrists corresponds to bone age of 12 years.

The child has continued to develop and since the age of a year and a half has had regular menstrual periods.

Dr. David Nabarro said that when the child Y. G. was found at the Great Ormond Street Hospital to have a positive Wassermann reaction, he was asked to see her and to give his opinion as to the advisability of giving the child anti-syphilitic treatment.

Although he had not himself previously seen precocious puberty associated with congenital syphilis, he had since been informed by Dr. S. L. Simpson that a positive serum reaction might be related to the condition, but that the majority of such cases did not have a positive W.R.

Dr. Nabarro thought it justifiable and worth while to try the effect of anti-specific treatment in this case and with this end in view the child was transferred to the Leatherhead Emergency Hospital in April 1946. She received 1.64 mega-units of penicillin in six days and a course of sulpharsphenamine was begun during the time the penicillin was being given. She was not benefited clinically, but the Wassermann and Kahn tests and the Price's Precipitation Reaction (P.P.R.) all improved after the first course of treatment. Owing to difficulties inherent in nursing and treating the patient, details of the subsequent treatment appeared not to be available.

Despite the fact that the serum reactions were positive on several occasions, from which it might reasonably be inferred that the child had syphilis, there was practically no confirmation of this. The mother had on several occasions given a negative blood test, the child is illegitimate, the father—with unknown W.R.—has returned to his own country and there are no sibs. The patient had never shown any sign or symptom of syphilis, congenital or acquired, except the positive blood reaction and the endocrine disturbance which conceivably might have a syphilitic aetiology. The six-year-old molars and central incisor teeth looked quite normal, though this was no evidence against congenital syphilis. Dr. Nabarro would suggest resuming treatment with arsenobenzenes and bismuth until blood reactions became permanently negative, though any further improvement in the patient's condition, should such occur, might be attributable to the continued effect of the operation on the ovaries and/or to the anti-syphilitic treatment suggested.

POSTSCRIPT (5.6.48).—Report on repeat blood test (Dr. Orpwood Price): "Routine Wassermann reaction positive. P.P.R. 5 units. Routine Kahn reaction negative. Compared with the results obtained two years ago she seems to be improving. Could you let me know if this is substantiated clinically?"

I am told by the Rampton doctor that she has improved very considerably, but as she has had about $\frac{2}{3}$ of her ovarian tissue removed, in addition to her anti-syphilitic treatment, it is difficult—if not impossible—to assess the value of either line of treatment separately. (D. N.)

Dr. Raymond Greene remarked that he was pleased to see again after an interval of some years, the patient, S. T. He had investigated this case, at the request of Dr. Bruce Williamson, when she was a patient at the Prince of Wales Hospital at Tottenham and he had come to the conclusion that her disorder was constitutional.

He drew attention to Novak's work on the subject of precocious puberty (*Amer. J. Obstet. Gynec.*, 47, 20, 1944). Novak had recorded 9 patients in whom menstruation had begun between the ages of 15 months and 7 $\frac{1}{2}$ years in whom no evidence of abnormal endocrine gland or of a cerebral tumour had been found. He pointed out that in constitutional cases, as opposed to those occurring as a result of granulosa-cell tumours, normal ovulation occurred.

Precocious puberty due to other causes than constitutional abnormality was excessively rare.

The Chairman (Mr. L. R. Broster) said that both sex precocity and diabetes insipidus were clinical entities following encephalitis lethargica which affect the region of the hypothalamus. Sex precocity of adrenal origin can be differentiated from that of hypothalamic origin by means of the 17-ketosteroid test. It is raised in the former and normal in the latter.

Obesity, Hypogonadism, Hypothyroidism, Adenoma of Thyroid Gland and Failure of Growth in a Girl aged 13 years.—RAYMOND GREENE, D.M.

Always rather plump but not considered abnormal in this respect until last summer when her mother noticed a lump in her neck. Weight has rapidly increased since then. She has not grown since age of 10, and shows no sign of onset of puberty. Intelligence normal.

Her father is tall and broad; mother of normal height, somewhat plump. One brother, aged 19, normal. No family history of thyroid disease.

She has had whooping cough and measles. There have been no accidents or operations.

On examination.—Very obese. Height 4 ft. 2½ in. Weight 6 st. 1 lb. Measurements: From vertex to symphysis pubis 2 ft. ½ in.; from symphysis to ground 2 ft. 2 in.; span 3 ft. 10 in. Skin very dry; in parts showed hyperkeratosis follicularis. Hands and feet small and fingers tapering. Breast enlargement due to fat, no signs of gland tissue. No body hair, pubic hair or axillary hair. Diffuse enlargement of the thyroid gland with nodule about the size of a walnut in right lobe. B.P. 100/60. Pulse-rate, during observation in hospital, varied between 64 and 84. Temperature 97° to 98.4°.

Investigations.—X-ray skull normal. B.M.R. —35%; after five injections of 1 c.c. of thyrotrophic hormone, —3.5%. Hb 72%. Serum cholesterol 364 mg. per 100 c.c. Glucose tolerance test: Fasting blood sugar 115 mg. per 100 c.c. After 50 grammes dextrose, 166 mg., 185 mg., 220 mg., 196 mg. per 100 c.c. at half-hour intervals. No reduction of urine throughout.

Diabetes Insipidus.—J. P. M. TIZARD, M.R.C.P. (for Dr. W. G. WYLLIE, M.D.).

M. S., aged 10 years 10 months.

First seen at the Hospital for Sick Children five years ago.

History.—At 5 years 10 months of age he had suddenly begun to suffer from excessive thirst and to pass large volumes of urine. He had to get up at night for drinks of water and frequently wetted his bed, having previously had normal control of micturition. His appetite was poor.

On examination.—Thin, weight 41½ lb. No abnormal physical signs in the nervous system or elsewhere. Fundi oculi normal. Urine: No sugar or albumin. Sp. gr. 1.012. Nothing abnormal on microscopy. Mantoux 1:1000 negative. Blood W.R. negative. X-ray of skull N.A.D. C.S.F. normal. Sodium chloride excretion test was suggestive of diabetes insipidus.

In hospital without treatment the fluid intake varied between 4 and 11½ pints per day and there was always nocturnal enuresis. On pitressin 4 minims daily the symptoms were not controlled and there were occasional reactions (pallor, abdominal pain). On pitressin tannate in oil 4 minims daily the fluid intake varied between 2½ and 10 pints and there was only occasional enuresis.

After discharge in June 1943 he continued the latter dosage, but by September injections every other day sufficed to control the polydipsia, polyuria and enuresis completely. One year later injections every third day were sufficient, but the following year the effect only lasted about forty-eight hours.

In December 1946 the treatment seemed less effective (? due to relatively ineffective drug) and he had to have injections twice a day. He was admitted to hospital. On admission he appeared healthy. No abnormal physical signs. B.P. 110/90.

On daily injections of ½ c.c. of pitressin tannate in oil the intake and output were reduced to about 50 oz. a day, but he developed attacks of abdominal pain and vomiting and a superficial glossitis. There were no ill-effects from the same dosage every other day and the urinary output was consistently below 5 pints a day. Since then his daily requirements have again changed and he is now having ½ c.c. of pitressin tannate in oil (2.5 pressor units) daily. His mother now says that polyuria precedes thirst by about half an hour. Micturition six to eight times a day. Now: Weight 67 lb. (expected weight 72 lb.); Height 52 in. (expected height 54½ in.).

Comment.—This child was shown to the Section of Pædiatrics by Dr. Wyllie in May 1943 (*Proc. R. Soc. Med.*, 36, 583. Case D). Apart from slight subcutaneous thickening in the thighs there has been no local reaction to the injections of pitressin tannate in peanut oil. In the past five years he has never had injections less frequently than once in three days.

It is interesting that the onset is sudden in such a high proportion of cases of diabetes insipidus, not only in those cases with sudden causative factors such as basal fractures and operations in the region of the pituitary fossa, but also in the idiopathic form. On the other hand slowly growing gliomata or craniopharyngiomata rarely produce diabetes insipidus even if they involve practically the whole of the hypothalamus (without incidentally the anterior pituitary being affected).

Section of the History of Medicine

President—Sir ARTHUR MACNALT, K.C.B., M.D.

[February 4, 1948]

Surgical Lectures of 150 Years Ago

By V. ZACHARY COPE, M.S.

SET courses of lectures purporting to cover the whole subject of Surgery have gone out of fashion. The subject is so vast and there are so many good textbooks that there is neither the possibility nor the need to give every detail in lectures. To some of us it is rather a matter of regret that any kind of set course of lectures in surgery is at the moment unpopular, for the spoken word has still many advantages over the written. One hundred and fifty years ago all or most of the facts of surgery could well be related in a course of lectures and in the absence of good textbooks it was necessary for each surgeon to give formal instruction to his pupils. Courses of lectures were usually given in the evenings. They were advertised and fees were paid by the students to the lecturer. Only a good lecturer was likely to obtain a good audience. Incompetence was never endowed. It is likely that some surgeons made considerable incomes from their lectures but at least one great surgeon did not lecture primarily to get money, for John Hunter made it quite clear that it did not pay him to lecture; he stated that he could easily earn more by pursuing his surgical practice; his reason for lecturing was at least partly to educate himself for, he said,

what more than all induced me to lecture was the great advantage every one finds by putting his thoughts in writing. A man can never tell how much he knows till he arranges his knowledge, and then he can tell how defective he is.

I have looked through the lectures of Cline, Pott, John Hunter, Abernethy and Astley Cooper of which there are many copies in manuscript in various libraries.

I found nothing to comment on or quote in the discourses of Henry Cline (1750–1827) who, though a pupil of John Hunter, did not teach more than the orthodox surgery of his time. Though he was reputed a successful lecturer his writings are devoid of originality, and are dull to read. Pott was a much more interesting teacher. Though for the most part he follows orthodox lines he does from time to time put in some philosophic remarks. Thus he stresses the importance of the knowledge of physic to a surgeon, derides the man who requires a multiplicity of instruments rather than a few simple ones, and criticizes commercialism in the profession. His remarks on the reading and writing of surgical books bear quoting.

Some by merely the perusal of books retained only theory. Those by far became the ablest surgeons in the closet and were apt in conversation, but in the practical part they were at a loss and frequently deficient. On the other hand those instituted or instructed by practice only,

without the use of reasoning or books to help them laboured under an equal disadvantage. They were able to perform an operation dextrously without knowing perhaps when it should be done or when it was necessary.

He gives advice to the student in his reading:

Writers of surgery may be divided into two classes, viz. those of general systems and those of particular diseases. The former have not time to fill up minute particular diseases. They do little more than give you the outlines and copy from one to another. The latter you should read more attentively and pay always more respect to writers of individual diseases, and at the same time pay a respect to yourself. Let your own judgement be accompanied with his system—comparing it with what your observation and practice show you and then act accordingly.

Pott was an excellent lecturer who laid stress more upon the practical part of his profession. His style was lucid and his outlook almost modern in tone. One would hardly think that the following passage was written one hundred and fifty years ago, yet it comes from Pott's lectures.

Surgery has within these fifty years been improved very much, but let not this excite your vanity but tend rather to excite your ambition by assiduity and study to further improvements, for no doubt some years hence our successors will be as much astonished at our ignorance as we at our predecessors.

John Hunter, Astley Cooper and Abernethy are in a class by themselves, a class in which Hunter was the master and the other two the pupils. Hunter was himself taught by Pott but everyone will agree with Sir James Paget's view that

though in practical surgery Pott generally appears more thoroughly instructed—with the science and the exposition of principles Hunter alone deals worthily.

The contrast between Hunter's lectures and those of others in his time is very extraordinary. It can best be illustrated by the remarks of Cline in his *Hunterian* lecture of 1824. He states:

I had the happiness of hearing the first course of lectures which John Hunter delivered. I had been at that time for some years in the profession, and was tolerably well acquainted with the opinions held by the surgeons most distinguished for their talents, then residing in the metropolis: but having heard Mr. Hunter's lectures on the subject of disease I found them so far superior to everything I had conceived or heard before, that there seemed no comparison between the great mind of the man who delivered them, and all the individuals, whether ancient or modern, who had gone before him.

Hunter's lectures are models of philosophic thought. He was certainly the only lecturer of the time who tried to make his pupils think and for that reason it is quite likely that his lectures may not have attracted so large an audience. His style of writing is not always so clear as that of Pott but he puts forward original views. To give one instance:—Hunter explains the phenomenon of referred pain clearly by diagram and satisfactorily though not quite so clearly in words.

A diseased part may sympathize with a diseased part, or a sound part with a diseased part... the impression on the mind, which does not accord with the sensation, as the liver and shoulder, has always been referred to sympathy; but I believe it is not properly sympathy, but a delusion of the mind, and perhaps may be produced in some such manner as this (shown in diagram).

Hunter's description of immunity is interesting:

The body, once affected by some stimuli, never forgets, as it were their action, and thereby is never again affected by that poison, as in the small-pox, measles etc.

Hunter had the gift of apt illustration from his own clinical experiences, as for example:

Many small wounds perhaps would do much better without any dressing than with... Almost all cutaneous sores do better without dressing, such as pimples. A young gentleman had a small pimple on his leg, to which a little ointment was applied and in a day or two the surrounding parts were covered with similar pimples; these being treated with similar applications spread until the whole leg was covered with them. When I was consulted and asked what was to be done. "Nothing." "How is that?" "Can anything be easier" I said, "Do nothing to the leg." "Then the stocking will stick to it." "Let no stocking be worn: put the boy on a pair of trousers." The advice was taken and the leg dried and healed up directly.

The interest of the lecture was often enhanced by references to contemporary surgeons—a method which is, for various reasons, seldom made use of to-day. In speaking of his operation for aneurysm Hunter commented:

Mr. Bromfield objects to every operation in this disease, and that, in the first place, from the immediate want of success in the operation, and from its being a disease of the whole arterial system: he says "I once saw this operation performed by a gentleman" (that's me, gentlemen) "upon the popliteal artery; but the difficulty of the operation, and the embarrassment which the operator underwent" [me again] "will, I dare say, deter him from performing it again"; but I am not so soon deterred, gentlemen . . . With respect to Mr. Pott's observations—but we must leave Mr. Pott to another evening, for he is tougher than the other a great deal.

What an excellent insight this comment gives us into the professional life of the time.

Humour was an ingredient of Hunter's lectures. I will give an example in which practical wisdom is mingled with disdain of current therapeutics. Hunter was lecturing on carbuncle and referred to a patient aged 70 years who had carbuncles on his back:

As neither bark nor calomel with opium had been of any service I said to David Pitcairn, Now do not let us permit this patient to be lost, while we are only using such means as experience has shown to be of little or no effect; for, David, this is a case more belonging to my province than to yours; and I being an older man than you, have seen more of them than you have, and can tell you, what perhaps you did not know, that we have no powers in this case that are known. Now David is a truly sensible man, and not governed by form; he therefore agreed but wanted to know where we were to begin. Why, with the first letter of the alphabet, and go through the catalogue of the *materia medica* so as we do not stop too long on the letter B, bark, as is the case in general.

In the event they tried *cicuta*, *sarsaparilla*, elm bark and caustic fossil alkali and the man recovered while he was taking the last two. Hunter related in his lecture how he had himself taken the alkali and since taking it had remained fairly free from boils to which he had previously been subject every spring.

Probably nothing interests a class more and certainly nothing emphasizes a point so decidedly as a personal reminiscence of the lecturer; Hunter frequently talked about himself in his lectures and I will quote one instance for it bears significantly upon his later illnesses.

Action of the vital organs may be suspended, and life continue, as was the case with myself. I had the gout in my feet three successive springs, and missed it on the fourth; when one day I was attacked with a pain so violent about the pylorus, as I thought, as no position could relieve; my countenance like that of a corpse. I took thirty drops of laudanum in tincture of rhubarb and found no relief; the pain continued, and upon examination I found no pulse, and at times found myself not breathing; I therefore forced myself to breathe. In this state I continued three-quarters of an hour: this went off gradually in about an hour, and have had no return of it since.

One could go on quoting from Hunter for a long time but I must get on to the lectures of Astley Cooper and Abernethy which really induced me to write this paper. My friend, Dr. Hobart Nixon, some years ago gave me a manuscript copy of notes of lectures taken by his great-uncle in 1824 and to this I am indebted for all the quotations from the lectures of Cooper and Abernethy. A perusal of the notes makes it clear that Cooper followed more the scientific side of Hunter's teaching while Abernethy talked little about the philosophy or science of surgery but gave very practical lectures interspersing them with numerous anecdotes and apt illustrations.

Abernethy used to treat a fracture of the femur with the patient lying on one side. He was a shrewd man and gave worldly-wise advice to his pupils. For example listen to him talking:

I remember a case that had all the symptoms of fracture as mentioned above, and the surgeon who attended the patient did not consider it as a fracture; however at last I was consulted and when I saw the patient I asked her "Did you put your foot to the ground after the accident?" "No, I could not for all the world." We then left the patient a short time to talk about the

nature of the case, and I said to the surgeon "What will the world say of you and me if we don't treat this case as a fracture and the woman should remain a cripple all her life? They will say we did not do our duty! What will they say if we do treat it as a fracture and she remains a cripple through life? That we tried every means and these were ineffectual". Then we laid the patient on her side, treated it as a fracture and she ultimately did well.

Abernethy's sound treatment of a gunshot wound by rest and simple dressings was enforced by this rather amusing case:

A gentleman living in town went to see some of his friends in the country and cockney-like went out to shoot sparrows, and cockney-like put his hand upon the muzzle of the gun, pulled the trigger and the contents went through the metacarpus; in this state a surgeon was sent for, and when he saw the case said—"it must be amputated or the patient will have tetanus, and then he'll die—but he might consult another surgeon if he wished".

A hospital surgeon was then consulted and he said—"I would not amputate for I have observed all sudden amputations after accidents prove fatal". Now if anyone could suppose that Job himself could have had two better comforters than these, he must, I am sure, have a superior imagination to mine. Well, in this difference of opinion I was next consulted as a referee and, seeing the case, I agreed that if the patient was likely to have tetanus it would be better to amputate; and then I agreed with the other surgeon—that sudden amputations after accidents were often fatal cases—but I said if I were the patient I would not have my hand removed, remarking that the parts injured were not very sensible, and that if kept quiet in splints, and supported in a tray, and inflammation of the more sensible parts kept off by the application of cold washes etc. the case would do well. The case was thus treated and the gentlemen were surprised to see how well it did—to be sure there was a little suppuration but the case did exceedingly well.

There is no doubt that Abernethy was a dramatic lecturer. He often emphasized his points by cases which, by the recorded wording, must have been related with great gusto and once heard would never be forgotten. I will give two examples, one concerning the treatment of retention of urine, and the other dealing with the reduction of a dislocated shoulder.

A young man fell from a garret window (having climbed up one night to see his sweetheart) and completely smashed his ilia and sacrum. I don't know how many fractures there were. However he was brought to the hospital, and I, being a "younger" was directed to draw off his water. I had done it three or four times when the nurse of the ward, an old woman, said to me "Lord bless you, young gentleman, you need not give yourself the trouble of coming to draw off his water, for I can make him piss when I like". I asked her how? She then thrust her fist on the lower part of his body making pressure and the urine flowed immediately.

The other case was related in these words:

I remember one summer going through the hospital square and I saw some of the pupils standing at one of the hospital doors rubbing their faces with their handkerchiefs, and were all of a perspiration, and they wished me to come and assist them. They had a dislocation of the shoulder-joint and had been trying to reduce it for more than an hour and were all tired; so I went to see the patient who was a coalman, and I never did see such a man in my life before; it was truly wonderful to behold the muscles that man had. It was certain the Pharnacian Hercules was not exaggerated; there were absolute hillocks of flesh. I said to the man "Will you allow me to try for seven minutes only? I shall not hurt you, and if I do not succeed in seven minutes I will not tease you any longer?" "Oh, yes sir." So I put a towel round the man's arm and made gradual extension. "Does this hurt you?" "Oh, no." "Well, I shall not hurt you, it will soon be right." I had not acted in this way long before the man called out "Lord bless you sir, that will never do, I, I'll put it off till tomorrow." "Nay" I said, "but you gave me seven minutes to try and I shall not try longer." At last he became more and more impatient and said "Lord bless you sir, I, I, shall fa- faint!" and it was in.

Nowhere have I ever read such an unforgettable account of the effect of steady prolonged traction in overcoming powerful muscular resistance. These extracts sufficiently show the qualities of Abernethy as a lecturer—not scientific nor philosophical but practical and dramatic.

Astley Cooper was probably the most able of the lecturers in the period we have chosen. He gave lectures which are even now interesting to read; they were based upon a sound anatomical knowledge and were often illustrated by the account of experiments on animals or by the recounting of clinical cases. He combined the

scientific with the popular. He had sat at the feet of John Hunter and he seems to have been imbued with something of his master's spirit. His lectures were probably more popular than Hunter's for he spent less time in theoretical disquisitions. Here are some extracts to show how interesting he could make his lectures. First there is his view on the question of the cause of inflammation:

It is generally said that air admitted into an abscess or into a wound will be productive of inflammation. Now air has no power to produce inflammation in the body. Dr. Haighton with a view to prove all this or to explain it took a living dog and made an opening in the tunica vaginalis testis (which has a direct communication with the cavity of the abdomen, but this is not the case in the human subject)—well, he made an opening in the tunica vaginalis and blew in air, till the abdomen became swelled and quite tense; in the course of a few days the swelling went down, and the dog quite recovered—however no inflammation followed. I think this an ingenious experiment of Dr. Haighton's. Air does not produce inflammation in wounds.

A young man who did not like the idea of going as a soldier endeavoured to make himself as it were a patient or sick person with a view to get off by going before a surgeon to examine him and say he was not capable of performing his military office; Well, what did he do? He made a very small opening in his scrotum, and then with a long pipe blew air in at the aperture which made a very large tumour indeed and appeared as if he had got an inguinal hernia—he walked nine miles to the surgeon and nine miles back again, but of course the surgeon was too well aware of the case as to be deceived. Still no inflammation followed this case. Inflammation can arise without the admission of air. It is the division of the vessels in the part that produces inflammation.

The story is a good one but the disproving of one theory merely led to the propounding of another quite as unlikely.

Cooper's colloquial style is well illustrated in the following:

The definition of adhesive inflammation consists in the effusion of fibrin whereby the parts surrounding become glued together. By this adhesive process cures are much sooner effected—in fact what cure would be effected without it? What was the state of surgery before Mr. Hunter found out this and published it? How widely different to what it is at this present time!

Formerly if a large portion of the scalp should be torn off from one part of the cranium by accident, O! The surgeon directly cut it completely off, for it was impossible so large a piece of scalp should again unite with the bone. Well, such was the practice once amongst the surgeons; and were they to arise from their graves and come amongst us now they would stand amazed. What if you were to be asked at the College "What would you do, sir, in a case where the scalp was torn off from part of the cranium? Would you say 'I would cut it off'?" Depend upon it, if you did you would be cut off too.

Most of us have read of the extreme anxiety displayed by Astley Cooper on the occasion of his removing a sebaceous cyst from the scalp of King George the Third; one may be able to understand his anxiety after hearing this story related in his lectures:

Wounds of the scalp are not so trifling as they at first might appear. Inflammation very often follows, erysipelas etc. and many die in consequence of the injury done to the scalp. . . . I will mention a case. I was called upon to remove a tumour from the scalp of a lady; it was unfortunately attached to the tendon of the occipito-frontalis muscle and I necessarily had to remove a part of this tendon. The operation was done on a Wednesday, she seemed quite well after its removal, but on the Sunday she was seized with rigor, succeeded by heat—she became feverish and on the Tuesday she died. Therefore you will I trust be upon your guard and never make an unnecessary cut on any part of the scalp for the practice is dangerous and you will not know what may follow such a wound.

We are all aware that Lord Lister introduced catgut into surgery but perhaps we do not all know that Astley Cooper tried the same substance for ligatures. Here is the account:

Different kinds of ligatures have been proposed such as those composed of animal matter, thinking they might become absorbed. In one or more cases I applied catgut round the arteries of a dog—and another of silk. I then closed the wound and allowed it to heal, but I cut off the ligature close to the artery. After a few days I cut down to the artery and I found that the silk ligature was detached or separated from the artery and was making its way to the surface; on the other hand the catgut ligature had separated itself and had buried itself in a kind of cyst. I know not how long this latter ligature might remain there before it became absorbed,

but perhaps it never would be absorbed. As for cutting the ligature off close to the artery you must not adopt this plan for in all probability ulceration will follow and also a tardy cure.

Cooper in his lectures was constantly referring to Hunter's work and he gave a full description of Hunter's operation for popliteal aneurysm; but the most interesting description is that which he gave of his own case in which he ligated the abdominal aorta. He explained that the aorta could become obliterated by disease without gangrene of the lower limbs resulting, and he had found that at least in dogs, the aorta could be ligated without serious damage to the lower limbs. He commented "tying the aorta is an operation that no man, I think, would covet". Concerning his own case he went on:

I do not know whether I should say anything about this, for you know there was a great deal said against me after I had tied this vessel—however I trust you may never have occasion to perform so terrible an operation.

Perhaps you may enquire "Would you do it again?" I answer "yes, tomorrow, if I had the opportunity", for I shall never be swayed or ruled by other people, by those who know nothing about the matter; I should listen to them as much as I should to the buzzing of a gnat or the hissing of a goose. The man on whom I tied the abdominal aorta had an inguinal aneurysm burst, and a violent gush of blood came forth, quite terrible to behold; well, was I to stand and see the man die from hæmorrhage when at the same time I thought I had it in my power to preserve his life? Certainly not, therefore I thought it my duty to tie the abdominal aorta, the only means left to save his life. I made a large semilunar incision in front of the abdomen taking care not to cut the umbilicus as this might occasion great pain. I made an opening into the front of the abdomen about four or five inches in length; then laying aside my knife I passed my finger down to the left side of the spine where I felt the vessel beating most famously, in fact at first it was appalling to me. I then carefully separated the artery from all the parts surrounding and succeeded in passing the needle round it; when the ligature was tied hæmorrhage ceased.

On the next day as I was entering the ward where the man lay, I was highly pleased, for I observed the man placing himself in a certain position as if preparing himself ready (for) when I came: I asked him how he felt himself? "Oh", he said "I feel very well sir, very well indeed. I have no particular pain." However the next day he died, but I never knew the cause of this sudden death. I really thought at one time the man would have survived the operation.

This dramatic incident is a fitting finale. In these brief extracts you will note most of the virtues which are peculiar to the spoken word. The emphasis laid on the essential point, the apt illustration to enforce the principle, the personal experience calculated to keep the student's attention, the dramatic demonstration, the witty allusion, the humorous story, even the sharp criticism of contemporaries—all these combine to make these discourses memorable. We have lost something by the abolition of such lectures.

Section of Surgery

President—Sir MAX PAGE, K.B.E., C.B., D.S.O., M.S.

[February 4, 1948]

DISCUSSION ON THE SURGICAL TREATMENT OF HYPERTENSION

Professor Robert Platt: Most speakers and writers on the subject of sympathectomy for hypertension conclude by saying that we cannot yet finally assess the results of this operation. That may indeed be true, but I think we know quite enough to say that sympathectomy for hypertension is a formidable and unphysiological procedure, that the results on the whole are disappointing, that the claims of surgeons must be accepted only after close and careful scrutiny; but that in some cases, which are quite unpredictable, a significant, lasting and beneficial reduction in blood-pressure is achieved.

That the procedure is formidable none I think would deny; that it is unphysiological is also self-evident. I do not like the word unphysiological but it is in common use, and is a brief and convenient way of saying that the procedure is one which does not restore normal function. Few operations do, but at least they closely approach this ideal in some instances, for example the removal of an insulin-adenoma, or a parathyroid tumour. The cause of human essential hypertension being unknown or unproved, an attack on purely physiological lines cannot yet be designed. Despite all the arguments which have been presented on the other side, I believe that the weight of evidence is in favour of a renal origin for essential hypertension. One cannot concisely summarize the reasons for this view and it must suffice to say that physiological studies in essential hypertension do not show it to differ in any significant respect from experimental hypertension due to renal ischaemia; neither can essential hypertension be distinguished by its effects from renal hypertension in the human subject. Vascular changes in the kidney can be found in over 90% of cases of essential hypertension (Talbot *et al.*, 1943) and clearance studies show a diminished renal blood flow. Although Goldring and Chasis (1944) make great point of the fact that this may be the result and not the cause of the hypertension, and that there is no evidence of ischaemia in the sense of a reduction in blood flow per unit of functioning tubular mass, this can be countered by the fact that similar findings are recorded in animals with experimental renal hypertension (Goldblatt, 1947).

For similar reasons the fact that neither renin nor hypertension has been demonstrated in excess in the systemic blood in chronic human hypertension cannot be used as an argument against the renal origin of hypertension, for these substances cannot be demonstrated in the chronic phase of experimental renal hypertension in animals, yet removal of the ischaemic kidney, or of the constricting clamp in these experiments, may cause a return of pressure to normal, which is surely proof of its renal origin.

Even if human essential hypertension is of renal origin, it is clear that its effects on the cardiovascular system are eventually serious, since most hypertensive patients die of cardiac failure or of cerebral vascular accidents. We are therefore justified in using unphysiological means to reduce the blood-pressure if they can be shown to have no serious untoward consequences. Sympathectomy seeks to reduce total peripheral resistance—and therefore to alleviate diastolic hypertension—by removing sympathetic tone from the splanchnic area and from the legs.

Mitchell (1947) has shown that in order to be reasonably certain of denervating the splanchnic area, the sympathectomy must extend as high as the fourth dorsal ganglion and as low as the second or third lumbar. This is more extensive than most of the operations performed at the present time. Denervated structures are hypersensitive to adrenalin (White and Smithwick, 1942) so that even a minimal remaining sympathetic nerve supply may, through its chemical effector mechanism, have widespread effects (Mitchell, 1947). These may be reasons why the results of sympathectomy are so unpredictable at the present time. Another reason why results are inconstant may be that sympathetic nervous tone is only one of several factors in the maintenance of peripheral vascular resistance. If one postulates that arteriolar contraction is a resultant of intrinsic vascular tone, sympathetic nervous tone and hormonal control (adrenal cortex), to which is added renal humoral control in hypertensive patients (fig. 1a and b), then sympathectomy will lower the blood-pressure by minimizing one of the factors (fig. 1c). But if, as seems probable, there is for each individual a maximal arteriolar constriction, which would seem usually to be represented by a diastolic pressure of 140 to 160 mm., and the sum of the factors already exceeds that which is necessary to produce this maximum contraction, then removal of sympathetic tone may have no effect (fig. 1d and e). This may explain the failure of sympathectomy in some cases of malignant hypertension but such an explanation is purely hypothetical and I would not wish it to be

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taken too seriously or my diagrams to be interpreted literally. They are not intended to illustrate quantitative relationships.

The same mechanism might account for the failure of depressor agents such as hypnotics and tetra-ethyl ammonium compounds to lower blood-pressure significantly in many of the severe cases.

Let us now examine the statements I have made on the results of sympathectomy, starting with my assertion that recorded results must be examined with close scrutiny before acceptance. Every physician knows that in many cases of hypertension there are wide, naturally

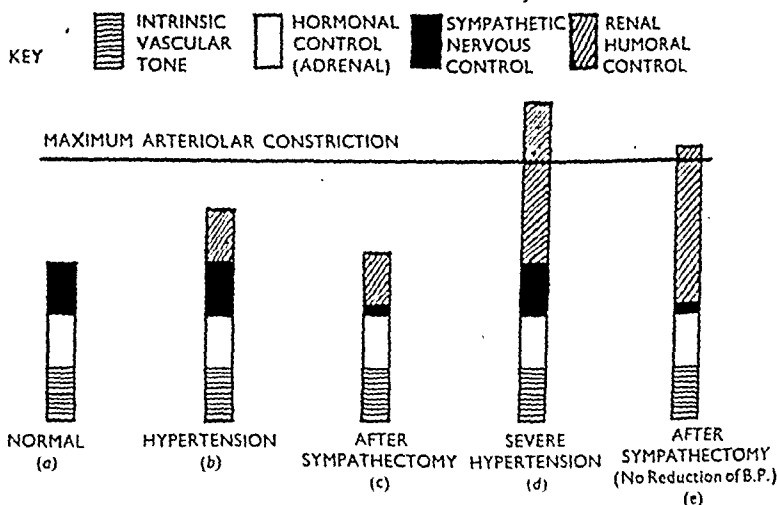


FIG. 1.

occurring, variations in blood-pressure. This seems to be especially true of the younger patients with essential hypertension, though I make that statement with reserve, as Hammarström (1947) throws some doubt upon it. Furthermore, there is considerable evidence that until the diastolic pressure has reached levels of at least 115 or 120, hypertension does not carry any increased immediate risk to life. All are agreed that women tolerate hypertension better than men, and we are all familiar with cases in which a severe, though often symptomless, hypertension has been sustained for several years without apparent progression or deterioration. Finally, in a large number of cases hypertension in its earlier stages is a symptomless condition, only becoming troublesome when an anxiety state is superimposed by the discovery of a high blood-pressure, so that we must beware of judging the result of an operation by its effect on symptoms. For all these reasons we cannot properly appraise the recorded results of sympathectomy unless we are informed of the age and sex of the patients, whether the blood-pressures quoted are maxima or minima and under what conditions they were taken both before and after operation. These data are not available in all or even in most of the published literature.

Of recent papers those by Poppen and Lemmon (1947), Palmer (1947) and Hammarström (1947) carry most conviction and my statements as to the results of sympathectomy are largely derived from them, supplemented by my own experience.

Results are bound to vary according to methods of selection, and for this reason I think that some of the statistically poorer results may represent a greater gain to the patients. For instance, if only cases of malignant hypertension were included, and if the operation was only successful in 10 to 20%, the results would be significant, whereas one is bound to be sceptical of claims of improvement even in 70% of mild cases of labile hypertension.

For these reasons I think that even as small a series as my own is instructive for each case is personally known and investigated. Our method of selection has been individual and, to a considerable extent, arbitrary. We have tried to exclude both extremes. On the one hand we have rejected elderly persons (most of those over 50) and those with poor renal function, advanced cardiac changes or serious cerebral complications. On the other hand we have refused to recommend such a serious operation to persons with only moderate elevation of diastolic pressure (for instance average levels of 110). Above all we have tried to assess what the prognosis would be without operation. If we felt that it was reasonably good we have discharged the patient after investigation, to be reassessed in say six months' time. Undoubtedly

such a selection is hard on the surgeon but it means that results obtained should be worth while.

The results we have tried to evaluate again on the grounds of prognosis. I have asked myself whether in my opinion the patient's diastolic pressure has been brought from a dangerous level to within a range of comparative safety. If so I have recorded the result as good. I have recorded as "worth while" cases in which there has been a significant fall of diastolic pressure (over 20 mm.) even though, because of high initial figures, the actual level is not as low as one would like. All the remainder I have recorded as failures. The actual figures are seen in Tables I and II and it is interesting that the average fall of diastolic pressure in the "good" results is not as great as in the "worth-while" cases, owing to the higher initial level of the latter group.

TABLE I.—RESULTS OF SYMPATHECTOMY (JANUARY 1948)

Still incomplete or too recent	10
Failed to complete operation owing to complication, &c.	4
Operative deaths	3
Failed (after complete operation)	9
Worth while result	8
Good result	4

Total 38

TABLE II

Group	Average age	Av. of max. and min. pre-op. pressure	Post-op. pressure (lying)	Change in diastolic pressure
Good (4 cases)	34	186/122	140/100	-22
Worth while (8 cases)	39	227/139	182/111	-28
Failed (9 cases)	35	210/129	225/132	+3

The series includes 8 cases of the malignant type of hypertension (with papilloedema). 2 of these failed to complete the operation owing to complications (both died later), 3 were unimproved (1 has died), the remaining 3 cases have all lost their papilloedema, with a significant fall of pressure in 2 and a considerable postural hypotension in the third, whose sympathectomy is still incomplete. The experience of seeing papilloedema resolve and blood-pressure fall in this otherwise intractable condition is a very gratifying one, even if good results are few and inconstant.

I have tried to see if pre-operative tests aid in the selection of patients. On our small series one cannot say that Smithwick's assertion is confirmed that a pulse-pressure of less than half the diastolic is a favourable sign. There is considerable evidence that a bad response to depressor tests with sodium amytal or pentothal will be followed by failure of the operation, but there are occasional exceptions. The cause of the hypertension does not seem to influence the outcome. Our favourable cases have included examples of chronic pyelonephritis and of hypertension following pre-eclamptic toxæmia.

The Smithwick operation was performed on the earlier cases in my series by Professor Geoffrey Jefferson or by Mr. H. T. Simmons. Lately Professor A. M. Boyd has been employing a more extensive operation. It is too early to say whether the results are better.

Finally a word on the permanence of the effects. My cases (all post-war) have been followed for a maximum of less than two years, but even in that time we find that those improved after six months have remained improved after eighteen months. Hammarström (1947) makes the same generalization after a follow-up period up to six and a half years in some cases, though Palmer (1947) finds that the number of successes becomes less as the years go on.

To the question as to whether sympathectomy is worth while I would therefore answer that it is, for it is the best we have to offer and can probably alter the prognosis of severe hypertension favourably in from 25 to 50% of cases. When the pressure falls, headaches and cardiac symptoms improve and retinal changes may clear up. Improvements in cardiac size and electrocardiogram are often recorded.

We might now consider what remains to be done. We still have to answer two questions of major importance, the first is whether an operation extending up to the fourth dorsal ganglion is better than the Smithwick procedure, and the second is whether the failures are due to failure of sympathectomy or failure to sympathectomize. In other words does hypertension persist in spite of denervation or because denervation has not been achieved? Professor Boyd has embarked upon an attempt to find the answers to these questions and I will not prejudge the results.

Sympathectomy for hypertension is a formidable procedure. The results are often disappointing because they are inconstant, unpredictable and difficult to assess, but in some cases a significant, lasting and beneficial reduction in blood-pressure is achieved. It is therefore worth attempting in younger patients where the prognosis without operation is judged to be unfavourable, provided that the case is not foredoomed to failure by renal insufficiency, severe cardiac or cerebral symptoms or advanced arteriosclerosis.

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Mr. D. W. C. Northfield: I propose to review our experience at the London Hospital of 46 cases of severe hypertension in which sympathectomy has been performed. This is a highly selected series of cases, for operation has been carried out only on those patients in whom the medical prognosis was known to be bad. The majority are cases of malignant hypertension or of renal disease with severe hypertension. Cases of uncomplicated benign hypertension have been avoided, owing to the impossibility of assessing prognosis in such patients. There were 39 patients (20 males, 19 females) with severe primary or essential hypertension, and 7 patients (4 males, 3 females) in whom the hypertension had developed secondary to renal disease. Five of the second group of patients had chronic nephritis, in one known to be of ten years' duration; one patient had bilateral hydronephrosis; and in one a nephrectomy for unilateral pyelonephritis and hydronephrosis had failed to improve his condition. The records will be analysed for the most part in three groups—males and females with essential hypertension, and cases of "renal" hypertension. All the patients have been seen by physicians, and for the most part by both Dr. Horace Evans and Professor Clifford Wilson who have a particular interest in these diseases.

In all these patients, frequent observations of the blood-pressure were made, though the sodium amylal test was not carried out. Routine renal function tests included urea concentration, blood urea, phenolsulphonphthalein excretion, and excretion urography. The fundi were examined by several observers, with special attention to the presence or absence of papilloedema, of hæmorrhage and of exudate, and the state of the retinal vessels. In many cases an E.C.G. and a cardiological report were obtained. Some patients had been under observation for a considerable period of time before operation, and this applies in particular to those with "renal" hypertension.

Using the state of the fundi as a criterion (Table I) the majority (approximately 80%) showed evidence of malignant hypertension although in some, judging by the known pre-operative duration of the hypertension, it seems probable that a malignant phase had supervened on a benign. Thus, in all 46 cases, normal fundi were present in only 4, and in only 3 others were the changes limited to tortuosity and irregularity in calibre of the arteries. In one-half (23) of the patients there was moderate or florid papilloedema; and in 14 others this was mild or doubtful, and in this group, with mild or doubtful papilloedema, there were also hæmorrhages and exudate in rather more than half. In two cases there were hæmorrhages and exudate without papilloedema. If the patients with hypertension secondary to renal disease are excluded, papilloedema to a greater or less degree was recorded in 33 of the 39 cases and it was more commonly present in males than females in the proportion of 20 to 13, though the sexes were almost equally represented (20 males, 19 females). Papilloedema was present in 5 of the 7 cases of renal hypertension.

TABLE I.—FUNDUS ABNORMALITIES

All cases	
4	Normal
2	Hæmorrhages and exudate
3	Tortuosity and irregular calibre of vessels
14	Papilloedema—mild or equivocal
23	Papilloedema—moderate to florid
46	

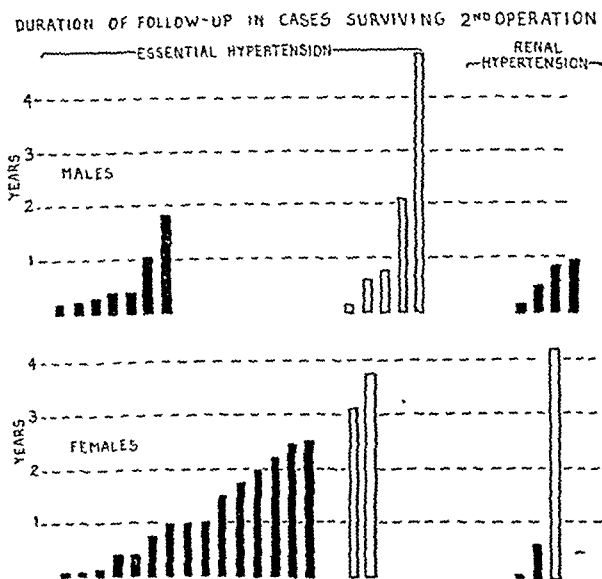
The hypertension was of a severe degree in many cases, the diastolic averaging 135 mm.Hg in the males and 131 in the females in the group of E.H.T. and approximately similar in the patients with R.H.T. To arrive at these figures, the lowest record during the month preceding operation has been selected, thus giving the patient the benefit accruing from rest in bed. The extreme figures were 190/100 and 140/110, on the one side, and 300/180 on the other; there were three patients with a diastolic pressure of 180.

The main features of the disease have been analysed in order to demonstrate their incidence in the patients with essential hypertension; this has not been attempted for the cases with renal hypertension as they are too few. Fundus changes of unequivocal degree are denoted

by P; evidence of disturbance of cerebral function, i.e. epileptiform attacks, loss of consciousness without convulsion, attacks of hemiparesis, transient or permanent, and mental deterioration by Ce; symptoms or signs believed to have indicated early or late heart failure by Ca; severe headaches by H; and impairment of renal function to a greater or less degree by R, assessed on the basis of all the tests of renal function. In each case a maximum of 5 can be scored, if the patient presented with all five features, and a lower score indicates less extensive manifestations; one must not read too much into these figures owing to the small number of cases, but the method may prove valuable in the future. Amongst the 20 males (Table IIa), 3 scored 5, 6 scored 4, 6 scored 3, and 5 scored 2; in the 19 females (Table IIb) the scoring was throughout on a lower level, namely, none scored 5, 2 scored 4, 9 scored 3, 5 scored 2, and 3 scored 1. This distribution of disease manifestations will be referred to again when reviewing results.

The Adson operation was employed until the end of 1943; this comprised a subdiaphragmatic resection of the splanchnic nerves and of the upper 2 or 3 lumbar sympathetic ganglia; 10 patients underwent this operation, with 2 operative deaths. In the remaining 36 patients the Smithwick operation has been carried out with 6 deaths; in this operation the ganglionic chain has been removed from T9 to L2 inclusive (with a few exceptions, in which T10 has been the upper level) and the great splanchnic nerves from a similar or higher level, to their termination in the coeliac ganglion. Comment upon operative details will be made later.

There were two patients with essential hypertension in whom the operation was not undertaken on the second side on account of their rapid deterioration as a result of the disease, and they died eighty-one days and ninety-six days respectively after the first stage, one from cerebral haemorrhage and heart failure, and the other from heart failure. There are 29 patients with essential hypertension who survived the bilateral operation and all have been "followed up" (fig. 1). Dealing separately with the sexes, of the 12 men 5 have since died, one enjoying a very active life for four years and ten months and another for two



years and four months. The results amongst the 17 females are rather better, for there have been 6 patients who have lived for two years or more; only 2 patients have died, and they survived three years and ten months and three years and two months respectively, living fairly actively. Combining the results of operation on the 29 male and female patients with E.H.T. we find that 8 of them survived for two years or more although half of these subsequently died. All patients with renal hypertension survived the operation and only 1 has died four years and four months later.

Let us return now to an analysis of all cases of E.H.T. including those who died of the disease or of the operation, using the symbols and marking according to the manifestations of the disease, headache (H), papilloedema (P), cerebral (Ce), cardiac (Ca), and renal (R) deterioration. The maximum marks for each case is 5.

TABLE IIA

MALES—E.H.T.

Deaths : operative	5	5	4	4	4	4	=	6 cases
subsequent	4	3	3	3	2	2	=	7 cases
N.B.—Those who died after two years four months and four years ten months, scored 2 each.								
Still alive	5	4	3	3	3	2	=	7 cases
N.B.—Longest duration one year ten months and one year one month, scored 3 each.								

The analysis according to the numbers of patients in each symptom group :

	P	Ce	Ca	H	R
Deaths : operative 6 patients	6	3	6	5	6
subsequent 7 patients	7	1	5	3	3
Still alive : 7 patients	7	3	5	7	1

TABLE IIB

FEMALES—E.H.T.

Deaths : operative	4	3	=	2 cases
subsequent	3	2 (at 3 $\frac{1}{2}$ and 3 $\frac{1}{2}$)	=	2 cases
Still alive : 4-3-3-3-3-3-3-2-2-2-1-1-1			=	15 cases
N.B.—Longest duration two and a quarter years.				

Analysis according to numbers of patients in each symptom group :

	P	Ce	Ca	H	R
Deaths : operative 2 patients	2	1	0	2	2
subsequent 7 patients	2	0	1	1	1
Still alive : 15 patients	9	6	9	11	3

In those dying from the operation there are more frequently to be found manifestations of the disease in all the important systems, and indeed operation might well be refused in a patient in whom there are papilloedema, present or past evidence of cerebral and cardiac deterioration, severe headache, and impairment of renal function. As would be expected, in those patients who survived for relatively long periods the incidence of the disease is generally manifested in fewer directions. These analyses and the operative mortality show that women prove better subjects, and that the disease is less severe in them. It is probably significant that renal impairment was much less frequent amongst the survivors, i.e. only present in one of the 7 males although all of them fell in the P and H groups and 5 in Ca group; and only present in 3 of the 15 females where 9 were in P group and 11 in H, and 9 in Ca.

The results may also be examined according to the fundus changes (Table III). Amongst the 20 males with essential hypertension there were 12 patients with moderate or florid papilloedema and of these only 3 survive, all recent cases (two, three and four months). Three died following operation, and amongst those who died subsequently, one lived for four years and ten months. There were 7 others with papilloedema which was mild or equivocal and of these 3 are still alive (one for one year and one month). One case in which there was no papilloedema but retinal hæmorrhages and exudates were present is alive one year and ten months after operation. In the group of 19 females, there were 8 with moderate or florid papilloedema and of these 5 still survive, to a maximum of two and a half years, and of those who died 2 patients survived for three years and ten months and three years and two months. Of 5 patients in whom the papilloedema was mild or equivocal 4 are living, up to a maximum of two and a quarter years. In the 7 patients with renal hypertension, papilloedema was moderate or florid in 3, mild or equivocal in 2 others; all are alive, except one who died four years and four months after operation.

TABLE III.—RESULTS IN CASES WITH PAPILLOEDEMA

MALES :

Moderate or Florid	12
Still alive (two—three—four months since operation)	3
“Operative” deaths	3
Subsequent deaths (maximum survival four years ten months)	6
Mild or Equivocal	7
Still alive (to a maximum of one year one month)	3
“Operative” deaths	3
Subsequent deaths (seven months)	1

FEMALES :

Moderate or Florid	8
Still alive (to a maximum of two and a half years)	5
“Operative” death	1
Subsequent death (after three years ten months and three years two months)	2
Mild or Equivocal	5
Still alive (to a maximum of two and a quarter years)	4
“Operative” death	1

No patient was refused operation solely on account of the height of the blood-pressure. Amongst the 20 males there were 6 with a diastolic pressure of over 150 mm.Hg (and in 3 it was 180) and of these only 2 are still alive one year and ten months and one year and one month after the operation; but one man with diastolic pressure of 180 lived for two years and two months after the operation. Amongst the 19 women, 5 had a diastolic pressure of 150 or over (maximum 160) and only one has died (an operation death). The height of the blood-pressure and its range shows no marked difference in the two sexes. In the group with renal hypertension the diastolic pressure ranged from 115 to 160.

In assessing the value of the operation, the effect on the blood pressure, on the headaches, on the fundi, and on general health will now be considered. There were 12 males with essential hypertension who survived the bilateral operation; in 8 the blood-pressure was not appreciably altered although survivals occurred to over two and four years; in 3 there has been a slight to moderate lowering and in 1 patient the pressure has been maintained at normal for four months. In the 17 females who survived the operation the pressure has been unchanged in 6 (survival up to three years ten months) there has been slight to moderate lowering in 5, and marked improvement in 6. In the group of renal hypertension the blood-pressure improved in 3, and has remained unaltered in 4. In all cases the record of the blood-pressure is the latest, and follow-up records show that although for a varying period after operation the pressure may be much reduced, as time passes it reverts more closely to its original figure. Headache has been greatly benefited in almost every case. Thus of 10 men in whom it was severe it has been abolished in 5, and much improved in 2, and in each of 13 women with severe headache it has been greatly reduced. In the 7 patients with renal hypertension, headache has been greatly improved in 6. The optic fundi were usually dramatically improved by operation, the papilloedema subsiding with consequent gain in visual acuity and exudates and hæmorrhages becoming absorbed. Changes of this nature occurred in 7 out of 12 male survivors (though 2 of these relapsed later), and in each of 11 women with essential hypertension, and in each of 5 patients with renal hypertension. General health and residual disability are not easy to assess but there is no doubt of the return of a sense of well-being, of physical and mental energy and endurance in many of the patients. In approximately half of the men and of the women there has been improvement of a worth-while degree—one man in particular worked very energetically for over four years. In the patients with renal hypertension, 5 of the 7 have shown improvement, the other 2 being still convalescent.

I would like now to direct attention to the 8 deaths following operation. Of these, two followed the lesser or Adson procedure and 6 the more extensive or Smithwick denervation. The ratio (1 : 3) is roughly the same as for the numbers of the two operations (10 to 36) so that although the Smithwick operation is undoubtedly the more severe it has not been followed by a heavier mortality rate. Admittedly the numbers are small for any generalization, and in the course of time we have learnt to reject cases which earlier might have been subjected to operation. Although these deaths are rightly ascribed to the operation, the manner of death shows that operation for the most part has but accelerated the morbid processes. In half, death was due to uræmia, although in one it was probably aggravated by a severe wound infection; a fatal outcome in these patients might well have been expected, for in 3 the pre-operative blood urea was 94, 106, and 125 mg. per 100 c.c. of blood respectively, and we have learnt not to operate on such cases. In the other case dying of uræmia, the pre-operative blood urea was only 56 but other routine tests showed a severe impairment of renal function. Two deaths occurred from heart failure, and in these the pre-operative blood-pressures were 300/180 and 230/180 respectively. There was one death from cerebral hæmorrhage five days after the first stage. The other death is ascribed to cerebral anoxia from hypotension; the blood-pressure steadily fell during the operation (second side) to a final reading of approximately 75, and a variety of resuscitative methods could not maintain it above 100 systolic for more than a few minutes at a time; after an initial recovery of consciousness when the anæsthetic was withdrawn, the patient passed into deep coma, areflexia, and hyperpyrexia of 106°, dying some fifteen hours after the operation. Necropsy confirmed the part played by anoxia. The pre-operative blood-pressure was not particularly high (220/130).

In attempting to assess the risk of operation in any particular patient, it is helpful to refer to the analysis of papilloedema, headache, and impairment active or past of cerebral, cardiac and renal functions (Tables II A and B). Operative deaths have occurred for the most part in those patients who presented with all five, or four out of five of these features, the women not scoring quite so high as the men (and they also carry a lower operative mortality). Those patients who survived the operation for the most part presented fewer of these features, i.e. only one scored the maximum 5 and only 3 scored 4, the rest scoring 3's or less. Therefore, in any particular case of essential hypertension, operation might well be refused if all five major manifestations are present, and certainly if the renal function is severely impaired;

a high blood urea of the order of 100 mg. per 100 c.c. of blood can be regarded as a single and unequivocal contra-indication to operation even if, in other aspects, the disease appears relatively light. But this last statement does not hold good for hypertension supervening on chronic nephritis, in which the body has apparently acquired some tolerance to the impaired renal excretion.

I have abandoned the subdiaphragmatic for the thoraco-abdominal operation for two main reasons. In the earlier cases in which the lesser denervation was carried out, the characteristic symptoms of postural hypertension were not encountered although blood-pressures were not then recorded in both the recumbent and the erect postures. This phenomenon is fairly frequent immediately after the Smithwick operation, denoting a more widespread territory affected by the denervation. Whatever may be the precise cause, whether the formation of a large somatic and splanchnic pooling of blood, or whether due to a diminished cardiac input, this more widespread denervation seems to offer a greater potentiality for reducing the blood-pressure, even though the effect is found to diminish with the passage of time. This appears to me to be one good reason for preferring this operation. My other reason is anatomical; it is difficult, if not fortuitous, to effect a complete splanchnic denervation from below the diaphragm. I have found that the great splanchnic nerve and the upper lumbar ganglia can be resected in a consistently thorough manner; but resection of the lesser and least splanchnics and of other variants in the sympathetic pathways is quite unreliable from below the diaphragm; whereas removal of their respective ganglia of origin ensures their severance. Anatomical studies by Sheehan and others have shown that the sympathetic system is liable to much variation in its details, and that residual pathways may frequently be the cause for relapse in conditions other than hypertension which are treated by sympathectomy. Therefore, to ensure that the splanchnic denervation is anatomically complete, the ganglionic chain must be removed in its entirety for a distance which includes that part which is liable to give off small known and unknown branches. In my opinion this is the most convincing argument in favour of a thoraco-abdominal approach, which affords adequate access for resection of the splanchnic nerves and of any other branches seen, and of the chain in continuity from T9 to L2 inclusive. Removal in continuity is important for, if the chain breaks, it is difficult subsequently to identify and to remove T12 and L1 ganglia, which are hidden under the diaphragm. It is recommended that the diaphragm be divided radially, but I find this unnecessary, and disadvantageous owing to the difficulty I have experienced in suturing it securely, as the sutures so easily tear out. Instead, I increase access into the thorax by removing the posterior few centimetres of the eleventh as well as the twelfth rib. This also allows a higher approach in the thorax, enabling the ninth thoracic ganglion to be exposed with certainty. I have found it unnecessary in most cases to divide the intercostal nerves; these can be preserved and do not usually obstruct the view, provided the musculovascular bundle is divided; I think intercostal neuralgia is less frequent if the nerves are preserved. A manœuvre described by Professor Paterson Ross, which facilitates the exposure and removal of the chain at the level of the twelfth thoracic and first lumbar ganglion, is to trace the lumbar chain upwards, splitting the crus over it for a few centimetres, and thus allowing proper identification of the chain and of its rami. The latter may run here for part of their course in an almost vertical direction, and it is easy to pursue a ramus in mistake for the main chain, and thus to lose the ganglion. An interval of at least two weeks has been allowed between sides, and often longer; delay has been occasioned most frequently by a pleural effusion, which though not mentioned in the literature so far as I am aware, has been the commonest post-operative complication, occurring after either side. These have been sterile (except in one case where it became infected from a wound infection) and have sometimes needed repeated aspiration before resolution. (In one patient the effusion persisted after many aspirations, and did not finally resolve until after the second operation.) Breathing exercises have, of course, been employed as a routine measure. In all cases I have assiduously attempted to avoid puncturing the pleura, not always successfully, because I have found that the operation is so much easier if the pleura sinks away with the lung. We have tried a variety of anaesthetics; the basis of all has been gas and oxygen with the support of pentothal, of cyclopropane, of curare, of a paravertebral block, and of a spinal analgesic. The ideal anaesthetic gives complete relaxation, quiet breathing so that the lung and pleura fall away, good oxygenation (for most of these patients have impaired cerebral circulation with little if any margin for anoxia), and avoidance of too sudden or too profound a fall of blood-pressure. I have found that shock or vascular hypotension rarely occurs at the first operation, but may be very severe at the second. Moreover, Dr. J. H. T. Challis and Dr. B. Kenton who have given most of these anaesthetics have noticed that during the operation on the second side, a fall of blood-pressure, sometimes of dramatic suddenness, is likely to occur when the identification and dissection of the splanchnics and sympathetic chain are commenced, or when they are cut. We have found that the best anaesthesia is provided by gas and oxygen with pentothal or with curare, the anaesthetist

controlling respiration during the intrathoracic dissection—this is a great help when stripping the pleura. In the more ill cases the splanchnic and the sympathetic chain can with benefit be infiltrated with local anæsthetic before starting the dissection. Spinal analgesia has been abandoned at any rate for the second side owing to the profound fall of blood-pressure which it is likely to cause. Severe hypotension at the second operation appears to be a potentially dangerous complication, and if it does not rapidly improve by raising the foot of the operating table and later of the bed vigorous measures should be taken to combat it.

I would like to record my gratitude to Professor Clifford Wilson and to Dr. Horace Evans for much of what I have learnt concerning hypertension, and for their helpful advice in these cases and in the preparation of this paper; and to Drs. J. R. Bolton and J. R. Ellis, Medical Unit First Assistants, for their help in analysing the case records.

Mr. F. A. d'Abreu: The discussion on hypertension held in the Section of Medicine in April 1947 (*Proc. R. Soc. Med.*, 40, 773) showed, I feel, that no method of treatment was generally agreed upon by surgeons or physicians. It is necessary, therefore, that surgical methods should be given careful testing under controlled conditions in investigating the effect of lumbodorsal sympathectomy on the more severe types of hypertension; the criteria we have adopted are: (1) retinal hæmorrhages and exudates with retinal œdema or papilloœdema; (2) a history of hypertensive encephalopathic incidents; (3) a fixed high diastolic pressure around 150.

All cases are included on one or more of these grounds. They are the ones which most urgently demand relief and have the gloomiest prognosis. They also include cases in which many authorities advise against operation and in which operation is said to give least benefit.

The report of the Metropolitan Life Insurance Company of New York, published in 1937, showed that half a million deaths occurred annually in the United States from hypertension, or at any rate from cardiovascular-renal disease with hypertension as its dominant symptom. After the age of 45 the death-rate from this disease is four times greater than that of cancer and twenty times that of tuberculosis or diabetes. Perhaps it is because the effects of hypertension are much less evident than those of cancer or tuberculosis that a more aggressive and combined attack upon the disease has not yet produced an agreed medico-surgical line of treatment. Also perhaps it is because the prognosis in each particular case of essential hypertension is unsure. The same reason cannot, however, be advanced in cases of the severe degrees of hypertension. Here, once the diagnosis is made, a fatal outcome is certain within five years and the vast majority will be dead in two years. Keith, Wagener and Barker followed up 146 malignant hypertensives on medical treatment alone and only one survived for five years.

In spite of the fact that Peet reported 19% of his malignant cases alive between five and eleven years after operation, it is this very group which so many authorities regard as being unsuitable for operation.

The horrors of the grave forms of hypertension are hard to exaggerate. The severe headaches, the rapid onset of blindness and an early and certain death with severe pain would, one might imagine, demand that every means should be taken to relieve the condition. If surgery can offer an alleviation of symptoms without certain proof of prolongation of life, it is clearly justified, if the operation carries with it no prohibitive mortality. If prolongation of life be attained the justification is even more evident.

The series of cases reported here is an attempt to examine the effect of sympathectomy in the different groups. It is important in the first place to define what one means by malignant hypertension as there appears to be some lack of agreement as to what constitutes malignancy. It has been said that one can only recognize it by the length of time which elapses between the onset of symptoms and death.

Recognition may be made on the following: (1) Sudden onset of gross hypertension in a previously normal patient. (2) Rapid progress of the disease. (3) A fixed high diastolic pressure. (4) Angiospastic retinitis with hæmorrhages, exudates and retinal and papillary œdema. (5) Cardiac and renal impairment.

The best cases to deal with are those with malignant hypertension and retinitis before cardiac and renal function are both significantly impaired. The word papilloœdema should, we feel, be reserved for cases with a space-occupying lesion within the skull. Retinal œdema, which may or may not involve the papillary area, is the sign which points out the gloomiest prognosis.

I hope to show in this small series of cases that operation should be performed in every case of the worst form of hypertension if severe kidney damage has not yet occurred. The

a high blood urea of the order of 100 mg. per 100 c.c. of blood can be regarded as a single and unequivocal contra-indication to operation even if, in other aspects, the disease appears relatively light. But this last statement does not hold good for hypertension supervening on chronic nephritis, in which the body has apparently acquired some tolerance to the impaired renal excretion.

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I have found it unnecessary in most cases to divide the intercostal nerves; these can be preserved and do not usually obstruct the view, provided the musculovascular bundle is divided; I think intercostal neuralgia is less frequent if the nerves are preserved. A manoeuvre described by Professor Paterson Ross, which facilitates the exposure and removal of the chain at the level of the twelfth thoracic and first lumbar ganglion, is to trace the lumbar chain upwards, splitting the crus over it for a few centimetres, and thus allowing proper identification of the chain and of its rami. The latter may run here for part of their course in an almost vertical direction, and it is easy to pursue a ramus in mistake for the main chain, and thus to lose the ganglion. An interval of at least two weeks has been allowed between sides, and often longer; delay has been occasioned most frequently by a pleural effusion, which though not mentioned in the literature so far as I am aware, has been the commonest post-operative complication, occurring after either side. These have been sterile (except in one case where it became infected from a wound infection) and have sometimes needed repeated aspiration before resolution. (In one patient the effusion persisted after many aspirations, and did not finally resolve until after the second operation.) Breathing exercises have, of course, been employed as a routine measure. In all cases I have assiduously attempted to avoid puncturing the pleura, not always successfully, because I have found that the operation is so much easier if the pleura sinks away with the lung. We have tried a variety of anaesthetics; the basis of all has been gas and oxygen with the support of pentothal, of cyclopropane, of curare, of a paravertebral block, and of a spinal analgesic. The ideal anaesthetic gives complete relaxation, quiet breathing so that the lung and pleura fall away, good oxygenation (for most of these patients have impaired cerebral circulation with little if any margin for anoxia), and avoidance of too sudden or too profound a fall of blood-pressure. I have found that shock or vascular hypotension rarely occurs at the first operation, but may be very severe at the second. Moreover, Dr. J. H. T. Challis and Dr. B. Kenton who have given most of these anaesthetics have noticed that during the operation on the second side, a fall of blood-pressure, sometimes of dramatic suddenness, is likely to occur when the identification and dissection of the splanchnics and sympathetic chain are commenced, or when they are cut. We have found that the best anaesthesia is provided by gas and oxygen with pentothal or with curare, the anaesthetist

TABLE III							
	Age	Sex	Duration of symptoms	Pre-operative B.P.	Interval	Post-operative B.P.	Post-operative course
T. E. ..	30	M.	7 months	205/135	6 months	180/135	Symptomless; no evidence of cardiac failure. Doing full work
T. G. A...	40	M.	3 months	260/160	5 months	170/125	Working hard—probably too hard. Symptomless
R. N. ..	42	M.	3 weeks	260/150	6 months	200/130	Symptomless
J. H. ..	48	M.	Hypertension known for 15 years. Symptoms for one year	210/120	5 months	110/80	Symptomless but tires easily
K. M. ..	25	F.	Headache for 5 years. Blurring of vision for 2 months	230/155	4 months	195/125	Vision improved. Has returned to work
E. C. ..	29	M.	5 months	210/145	3 months	200/135	Doing light duties. Symptoms much improved. Occasional mild temporal headache
H. C. ..	47	M.	6 weeks	250/150	1 month	230/160	Died 11 weeks after second operation
W. D. ..	34	M.	2 years	250/150	6 weeks	170/130	Residual left visual defect. Occasional mild left-sided headache

Mr. King, the ophthalmic surgeon, very kindly examined all cases before and after operation and his reports on the fundi are given in Table IV:

TABLE IV			
	Pre-operative ophthalmic examination	Time interval	Post-operative ophthalmic examination
T. E. ..	Fundi: Veins congested and compressed by arteries at crossways. Many soft exudates along course of vessels. Only a few punctate hæmorrhages. Some retinal œdema. Well-marked hypertensive retinitis of grave general significance	3 months	The improvement in this man's fundi is striking—(a) all the recent soft exudates have disappeared; (b) the few small hæmorrhages have absorbed; (c) the venous congestion and retinal œdema are definitely less; (d) the small more chronic exudates near the optic disc in the right eye are smaller and less numerous
T. G. A...	Left fundus: Disc normal. Small white exudates between disc and macula. One cotton-wool patch along left infero-temporal vessels. Right optic disc not well seen. No papillœdema	6 months	Fundi normal
R. N. ..	Extensive hæmorrhages and exudates in right eye. Some hæmorrhages and exudates in left eye. Marked hypertensive retinopathy with thrombosis of inferior temporal vein	7 months	Improvement in the fundi is dramatic. On the right side there are exudates still present near the optic disc and one tiny hæmorrhage to the inner side of the optic disc. On the left side there are no exudates seen but two very small hæmorrhages along the superior temporal artery. There is sclerosis of arteries and veins
J. H. ..	Not seen by Mr. King		Not seen by Mr. King
K. M. ..	Both fundi show (a) tortuosity of vessels; (b) venous congestion; (c) diffuse retinal œdema; (d) a number of large exudates; (e) a few small hæmorrhages. This is a classic hypertensive retinitis	4 months	The improvement in the fundi is striking. The only pathological changes remaining are slight œdema most marked at the right fovea and a few points of exudate

prognosis in the untreated case of lesser degrees of essential hypertension is largely uncertain in each particular individual although there is a great deal of evidence, according to Peet, Smithwick and others, that the average expectation of life is appreciably lengthened by sympathectomy. The selection of cases in this group is important, and tests by sedation or epidural block show that some cases will not benefit by the operation.

In the group of severe cases treated by us none has been excluded whatever may be the result of sedation tests. All have received great benefit except one case who was submitted to operation when he was going blind and had very severe renal damage. He stood the operation well and said he felt better. This was the only case, however, in which no improvement in the fundi was seen. He left hospital but was readmitted some months later and died of cardiovascular-renal failure, having been almost completely blind for a month before his death.

All the cases have been treated by a team consisting, first, of a physician. Most of the cases were very fully assessed by Sir Arnold Stott and Dr. S. P. Meadows at the Westminster Hospital and reassessed after operation by them. The assessment by a physician is important for many obvious reasons and also has the advantage that a true and unbiased picture of the value of the operation may be formed. Another important member of the team has been the ophthalmic surgeon, Mr. E. F. King, who in every case but one reported on the fundi before and after operation and has provided us with paintings of the fundi [shown at the meeting]. The anaesthetist, Dr. G. S. W. Organe, has discovered, by careful investigation of the patient under anaesthesia, some interesting facts about the disease. A careful follow-up is, of course, essential.

All our cases, except the one mentioned above, who was, I must admit, treated somewhat experimentally to determine the degree of renal impairment beyond which the irreversible change occurred, have returned to work and are asymptomatic. The series, though small, ranges between the ages of 25 and 48 and there has been no operative mortality. These two facts make us feel certain so far that there can be no question of the value of sympathectomy in the most serious forms of hypertension.

The Smithwick type of sympathectomy has been used in all, fulfilling what we regard as the minimal excision, i.e. from T8 to L1 at least, on each side, with excision of the coeliac ganglion and the greater, lesser and least splanchnic nerves as high up as possible. This operation is safe and no severe complications have occurred post-operatively. It is pre-ganglionic and although the sympathetic chain cannot be removed at as high a level as by the transthoracic route, a very full and complete excision of the coeliac ganglion is done and by excision of the eleventh as well as the twelfth ribs, the sympathetic chain can be removed as high as T7. The higher level, which can be reached by the transthoracic route, is not absolutely necessary as far as the splanchnic nerves are concerned as these are only relayed in the sympathetic chain, their ganglion being the coeliac. Another advantage of the Smithwick approach is that the kidney can be fully explored, tumours of the suprarenal excluded and all the sympathetic filaments to the adrenal gland removed also. A biopsy of the kidney can be made when required.

The dissection is extrapleural and the only post-operative complications have been pleural effusions which, except in two cases, have been minimal. In two cases also there has been severe referred neuralgic pain into the loins and inguinal regions. This pain has always cleared up in a fortnight at most and has always been helped by getting the patient up.

All cases are subjected to the following pre-operative investigations:

TABLE I.—ROUTINE PRE-OPERATIVE INVESTIGATIONS

- | | |
|-----------------------------------|--|
| (1) X-ray and screening of chest. | (5) Examination of urine. |
| (2) Intravenous pyelography. | (6) Examination of fundi and painting. |
| (3) Electrocardiography. | (7) Serial blood-pressure estimations. |
| (4) Kidney function estimation. | (8) (Sedation reaction.) |

TABLE II.—SYMPTOMATOLOGY

	T. E.	T. G. A.	R. N.	J. H.	K. M.	E. C.	H. C.	W. D.
Headache ..	+	+	0	+	+	+	+	+
Impairment of vision ..	0	0	+	0	+	+	+	+
Dyspnoea ..	+	0	0	0	0	0	0	0
Encephalopathy ..	0	0	0	+	0	+	+	0
Fatigue ..	0	+	0	0	0	0	0	0
Hæmoptysis ..	+	0	0	0	0	0	0	0

The preliminary results of operation may be seen from a study of the following summary of the cases. The pre-operative blood-pressure was taken after a period of rest in bed and the post-operative blood-pressure was taken with the patient lying down on a couch when attending as an out-patient (Table III).

cutaneous area of anhidrosis by means of an extremely sensitive electro-dermatohmeter designed by A. H. Ratcliffe.

Fig. 3 shows the best pattern yet found and fig. 4 the worst. In each case the anatomical

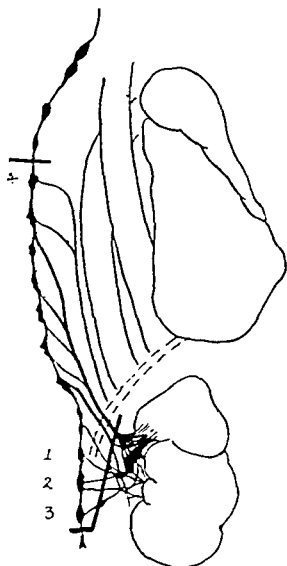


FIG. 1.

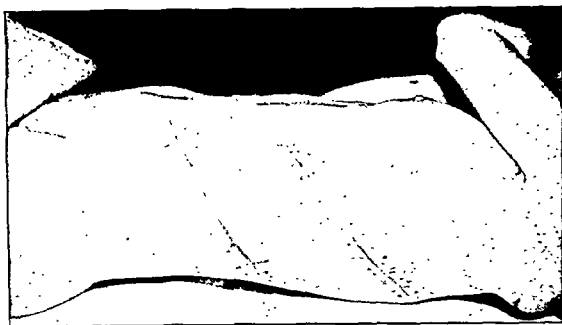


FIG. 2.

FIG. 1.—Diagram showing the extent of sympathectomy for hypertension.

FIG. 2.—The incisions for extensive thoraco-abdominal sympathectomy.

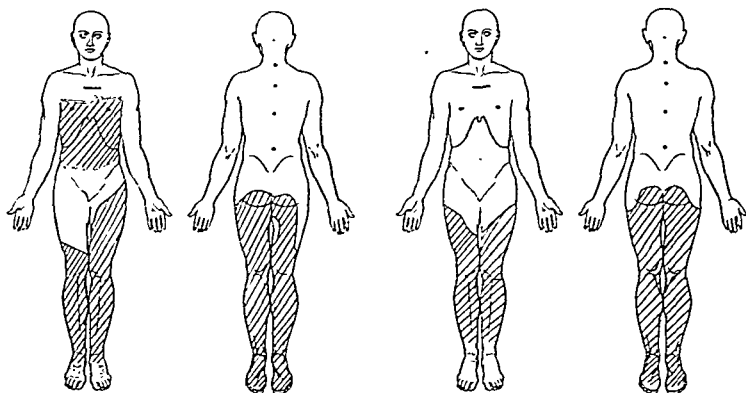


FIG. 3.—Cutaneous area of anhidrosis after removal of the sympathetic trunks from above T4 to below L3. Good pattern.

FIG. 4.—Poor pattern following the same operation.

removal has been satisfactory, but careful examination with the electro-dermatohmeter has revealed incomplete denervation. It is felt that unsuccessful results of sympathectomy in hypertension may be due to incomplete denervation rather than to the selection of an unsuitable type of hypertension.

Mr. A. Dickson Wright: There is no doubt that sympathectomy supplies a means of breaking the vicious circle which obtains in hypertension, and now that the operation has proved successful in the younger cases, there has been a tendency to extend the operation to greater ages than ever, 55 or 60 in selected cases, and also to practise the operation in cases with definite signs of cardiac mischief. Northfield seems to have been operating on cases which I have been in the habit of refusing as being too risky and hopeless, and seems to have salvaged some of these cases. The choice of operation is now very difficult, good results having been claimed with all of the operations. A useful clinical experiment would

TABLE IV (*continued*)

	Pre-operative ophthalmic examination	Time interval	Post-operative ophthalmic examination
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E. C. . .	Both fundi show (a) a few soft exudates and striate hemorrhages; (b) congestion of retinal veins; (c) silver wire arteries; (d) generalized retinal oedema. A case of hypertensive retinopathy	5 months	The improvement in both fundi is marked. In both eyes all hemorrhages have disappeared and all soft exudates absorbed. There are, however, some small hard exudates above the right macula which are new. The retinal oedema is much less marked though still visible round the optic discs. The vessels are unchanged
H. C. . .	Fundi: Gross retinal oedema, exudates and hemorrhages. Swelling of optic discs not excessive. Arteries and small veins congested and irregular. Gross hypertensive retinopathy affecting particularly the optic discs, and peripapillary areas		Died eleven weeks after second operation
W. D. . .	Fundi: (1) Retinal oedema particularly around macula and optic discs; (2) sclerosis of arteries which show extreme variability in calibre; (3) veins somewhat congested and compressed by arteries at crossing; (4) a few medium "soft" exudates round macula; (5) no hemorrhages; (6) widespread anterior choroid-retinal degeneration. This no doubt is partly due to retinal vascular changes, but also to underlying sclerosis of choroidal vessels	2 months	Very considerable improvement. The arteries are still constricted but there is now no nipping of the veins. On the temporal side there are a few residual patches of exudates otherwise the retina there has returned to normal. Mild oedema on the nasal side of the disc

This series with so short a follow-up does not, as yet, advocate operation on the grounds of prolongation of life, but the fact that these seriously distressed and incapacitated people are now all, except one case, asymptomatic and back at work, convinces us of the value of sympathectomy in severe hypertension. Unless these first cases are quite abnormal we feel that one might as well refuse to remove a painful cancerous growth because ultimate cure or freedom of symptoms could not be promised, as deprive these unfortunate cases of the relief afforded by an adequate sympathectomy.

I would like to express my thanks to Sir Arnold Stott and the physicians of the hospital for the assessment of these cases and for asking me to operate on them, to Mr. King for his great help with the ophthalmoscopic aspect and to Dr. J. Harland and Mr. C. Drew, the respective medical and surgical registrars, who have done so much in keeping the records of these patients.

Professor A. M. Boyd: Surgeons perform sympathectomy for hypertension with differing objects in view. Some maintain that sympathectomy acts by producing passive dilatation over a wide area of the vascular bed with consequent decrease in peripheral resistance. Others stress denervation of the suprarenals with diminution in secretion of adrenaline or interception of vasoconstrictor impulses to the kidney as their objective.

As the cause of hypertension is still illusive, the rationale of sympathectomy must be conjectural. It is probably wise to plan a sympathectomy which will achieve all the suggested requirements. Professor G. A. G. Mitchell of Manchester, on anatomical grounds, has shown that in order to be reasonably certain of meeting these requirements, bilateral resection of the sympathetic trunks from the fourth dorsal ganglion to the third lumbar and removal of the splanchnic nerves are necessary. The fourth dorsal ganglion must be removed in order to be certain of including the para-aortic nerves (Mitchell). The third lumbar ganglion should be included in order to remove contributions from this ganglion to the renal plexus (fig. 1).

I have carried out this procedure since January 1947. The twelfth dorsal ganglion to the third lumbar are removed through an oblique muscle-cutting incision in line of the twelfth rib, part of which is resected. The upper segment and thoracic splanchnics are removed transpleurally, access being gained by resection of the eighth rib (fig. 2). An attempt has been made to estimate the completeness of the operation by careful mapping out of the

Clinical Section

President—G. E. VILVANDRÉ

[February 13, 1948]

? **Gummatous Ulceration.**—J. H. B. URMSTON, M.R.C.S., L.R.C.P. (for T. W. MIMPRISS, M.S.).

E. L., aged 53, presented as a case for diagnosis.

She has noticed a "lump" on the face for three years. Healthy, has never been abroad; had two miscarriages and has one son aged 23 alive and well.

History of three years' duration—difficult to obtain. Three years ago had an ulcer of cheek which spread destroying the right orbit. This was followed by a swelling which descended from her forehead. She has no other complaints and has had, until reporting to hospital three weeks ago, no treatment whatsoever.

On examination she has an œdematous swelling arising from the upper lid of the right eye, the size of an orange. The right cheek was perforated by various sinuses discharging yellow pus—the right eye was not visible. There was scarring over the front of the neck, presumably where the process had healed.

Nothing else relevant in general examination was discovered.

Special investigations.—W.R. ++. Kahn +. Urine: Albumin a trace.

On microscopy of discharge from lesion—no lepra cells or mycelia seen.

X-ray of skull: Evidence of basal sclerosing osteitis.

Mr. Mimpriss: The scarring on the left-hand side and front of the neck shows that healing has occurred in places. This, in my opinion, excludes the possibility of a malignant process. The scarring here is typical of a healed gummatous ulcer.

There is no further clinical evidence to support this diagnosis but an X-ray of the skull shows a change in the base which is compatible with a gummatous osteitis. The serological tests are positive and a fortnight's treatment with mercury and iodides has produced some improvement. For these reasons the diagnosis of a gummatous ulceration seems the only possible one.

Angiocardiography in the Diagnosis of Congenital Heart Disease.—K. D. KEELE, M.D.

Angiocardiograms of three cases of congenital heart disease were shown. The following is one illustrative case.

History.—M. H., a boy aged 5 years. During his first year the patient had occasional attacks of asthma, which have become less frequent. He has not been cyanosed, and has had no other symptoms. Plays games vigorously.

Examination shows a well-built boy; normal size; weight 42 lb.

Heart: Apex beat in nipple line. Systolic thrill over aortic base. Loud systolic murmur, maximal at aortic base, conducted along the carotids, and heard posteriorly on the left. B.P. 110/80.

Arteries: Femoral pulses palpable but diminished. No evidence of anastomotic vessels even on bending forward. Other systems normal.

be to re-operate on some of the Adson and Peet operative failures, and remove the ganglionic chain transthoracically, and endeavour to obtain further facts, and it is quite possible that the cervical sympathectomy obtained by the transthoracic operation, might lessen the risks of cerebral and ocular hæmorrhage, by facilitating the flow through the other branches of the aorta. The main danger of these extensive sympathectomies is a period of post-operative cerebral ischæmia, which causes neuronal damage in the brain. Great care in the early post-operative days after the second operation is essential to maintain the blood-pressure at an adequate level by intravenous saline containing adrenaline or ephedrine.

Professor Clifford Wilson: I wish to stress the importance of accurate diagnosis in patients subjected to sympathectomy. Hypertensive renal disease is traditionally a confusing subject but recent work has thrown considerable light on the natural history of the different forms of Bright's disease and has made the assessment of prognosis less uncertain. I was glad to see that the openers had all selected for sympathectomy patients with a grave prognosis. In benign hypertension the prognosis in the individual case is an unknown factor; in malignant hypertension the average duration after the diagnosis has been made by the finding of papill-œdema is one year. It is therefore impossible to estimate the value of sympathectomy in mixed series of hypertensive patients such as have been described by some American writers. In malignant hypertension the prognosis is so grave that operation is justifiable even though the percentage of successes is discouragingly low. I must, however, emphasize the importance of papill-œdema as the diagnostic sign of malignant hypertension. In Mr. d'Abreu's series this diagnostic criterion of malignant hypertension; the only fatal case was one of these. There is a tendency to regard the result of sympathectomy as a failure if the blood-pressure level does not fall appreciably. In many instances, however, the hypertension changes in quality even though it remains quantitatively unaltered; that is the malignant character of the disease, which leads to retinal changes, increased intracranial pressure, renal vascular lesions and left ventricular failure, may be modified so that the hypertension becomes relatively benign. Unfortunately this alleviation is in the majority of cases shortlived, and it is understandable that the surgeon prefers to operate on severe cases of benign hypertension, where, although the natural outcome is uncertain, the effect of sympathectomy, especially in women, is more impressive and more lasting. I am of the opinion that the attempt to break the hypertensive vicious circle is well worth while even in patients with chronic nephritis or pyelonephritis who are on the verge of renal failure. In these cases there is often a steep rise in blood-pressure before renal function tests deteriorate; operation at this point can bring about a reversal of retinal changes and, as Mr. Northfield's cases have shown, can postpone the uræmic termination. In our series these patients have proved good surgical risks even when there was moderate nitrogen retention (up to 100 mg. %).

Dr. G. S. W. Organe showed blood-pressure and pulse records of patients with hypertension undergoing Smithwick's operation under general anæsthesia. These showed violent fluctuations not seen with other patients and less marked in the less severe cases. Commonly, there was a severe fall with a narrowing of pulse-pressure—from 260/190 to 125/120 in one case and from 220/160 to 115/105 in another. He thought this of an increased pressure gradient to the brachial artery, due to spasm of arteries proximal to the elbow, rather than to a fall in the head of pressure at the centre. Intravenous injection of 200 mg. of procaine, minutes, to 210/170 in the first and to 185/150 in the second case mentioned above. If the brachial pulse-pressure fell again, it could again be improved by injection of procaine but not always as markedly as at first. In a healthy patient, whether or not he was anæsthetized, intravenous injection produced some tachycardia but not a rise in blood-pressure.

[March 3, 1948]

THE following Short Papers were read; the Honorary Editors regret that present-day exigencies of space preclude the publishing of a full report:

Crohn's Disease.—By HAROLD C. EDWARDS, C.B.E., M.S. Those taking part in the discussion were Mr. Guy Blackburn, Mr. E. G. Tuckwell, Mr. A. Dickson Wright, Mr. J. P. Hosford and Mr. E. C. B. Butler.

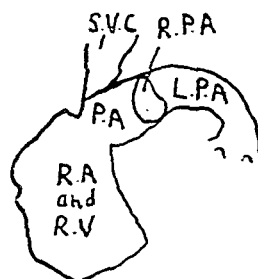
Obstructive Factor in Sialitis.—By B. MCN. TRUSCOTT, M.B.E., F.R.C.S. Those taking part in the discussion were Mr. E. G. Tuckwell, Mr. A. Dickson Wright and Mr. Sol M. Cohen.

Intermittent Claudication.—By R. P. JEPSON, M.B., B.Sc., F.R.C.S. Those taking part in the discussion were Mr. Peter G. C. Martin, Mr. Sol M. Cohen and Mr. J. P. Hosford.



FIG. 3.

the right pulmonary artery is seen end-on as a dense opacity within the shadow of the main artery.



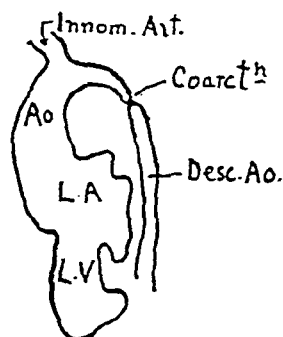
(2) *Left Anterior oblique view:* Film 2 taken at 3 sec. (fig. 3). This film corresponds in timing with film 2 in the A-P view. It shows filling of the right side of the heart. The superior vena cava can be seen entering the right auricle. The shadow of the right ventricle is superimposed on that of the auricle, and probably cannot be distinguished from it in the reproduction. The main pulmonary artery, and left pulmonary artery arching backwards, are clearly seen. In this view



FIG. 4.

direct evidence of coarctation. There is no evidence of an accompanying patent ductus arteriosus.

Dr. Keele also showed a case of pulmonary stenosis and patent ductus arteriosus



Film 6 taken at 9 sec. (fig. 4) shows filling of the left auricle and ventricle. The ventricular septum is clearly seen. From its upper end the ascending aorta is seen arching forward. The innominate artery is seen coming off the aortic arch. At the commencement of the descending aorta there is a rapid spindle-shaped narrowing of the aorta with dilatation distally—

X-ray (screening): Large left ventricle. Aortic knob well seen, no evidence of rib erosion on film.

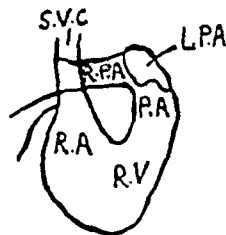
Electrocardiogram: Normal limb and chest leads.

Angiocardiogram (*see figs.*).—(1) *Antero-posterior view*: Film 2, taken at 3 sec.



FIG. 1.

Its descending branches may be seen near the left border of the heart.



(fig. 1). This film shows filling of the superior vena cava, which can be followed into the right auricle. The input tract of the right ventricle flows horizontally to the left. The output tract flows upwards completing the third part of a U-shaped curve to the pulmonary artery. The bifurcation of the pulmonary artery is seen with the right branch crossing the spine and entering the right hilar region. The left pulmonary artery, as it passes backwards, forms a dense opacity within the shadow of the main artery.



FIG. 2.



Film 4 taken at 6 sec. (fig. 2). The pulmonary veins are now filled, and are seen converging on the left auricle which forms an oval opacity in front of the vertebræ. A narrowing of this shadow to the left indicates the region of the mitral valve. To the left and below this the left ventricle can be seen. It is not clearly outlined except in its upper part, a sign of its being in systole. The large ascending aorta is clearly seen.

X-rays: Tumour in anterior mediastinum (figs. 1 and 2).

Bronchoscopy: N.A.D. Diagnostic pneumothorax. Exploratory thoracotomy (Mr. T. Holmes Sellors): Tumour in anterior mediastinum, hard and infiltrating surrounding structures to which it was densely adherent. It was inoperable. Biopsy taken. Subsequent course uneventful.

Histology: "Section shows strands of cellular infiltration between fibrous tissue. The cellular areas show very large numbers of eosinophilic polymorphs. There are giant cells with large pale vesicular nuclei and opaque cytoplasm. There are occasional giant cells with three or four nuclei.

"These appearances probably represent Hodgkin's disease in the sclerosing stage."

Splenomegaly: Tuberculoma of Spleen. Benign Hypertension.—R. W. BAZELEY, M.B., B.S. (for J. BROWNING ALEXANDER, M.D.).

F. H., male, aged 44. Has never been abroad. No previous history of illness apart from fractured left ribs in 1940.

History of present condition.—Onset December 1946 of tightness in upper abdomen and pain under left costal margin. Symptoms relieved after one week in hospital, but recurred.

8.4.47: Ruddy, healthy: weight 10 st. 10 lb. Pulse 72, regular. Heart: Apex beat fourth space, one inch outside mid-clavicular line. No murmurs. B.P. 240/100. Bulging of left lower chest and obvious bulging of left hypochondrium. Spleen: $4\frac{1}{2}$ in. below left costal margin; slightly tender on palpation. No bruit. Liver margin just palpable, but not tender.

Other systems normal.

Investigations.—Blood-count 10.4.47: R.B.C. 4,700,000. W.B.C. 11,000. Polys. 75%. No abnormal red or white cells. Sternal puncture: Marrow count within normal limits. Blood W.R. negative. Chest X-ray: Small rounded opacity continuous with left eighth rib (? old trauma). Small, well-defined circular opacity in left mid-zone, possibly a secondary, but most likely a fibrotic nodule.

Progress.—3.5.47: Barium meal: Stomach displaced to right of spleen, which produced a filling defect in greater curvature by pressure. Splenic enlargement and discomfort gradually decreased, and on 7.5.47 spleen $2\frac{1}{2}$ in. from costal margin. Weight unchanged. Patient afebrile throughout. Discharged from hospital.

December 1947: Well and working, but appetite poor. B.P. 170/110. Spleen enlarged 4 inches. Barium meal: Alimentary tract normal. Mass pressing on stomach from left. Large calcified shadow in left upper abdomen. ? calcification in (1) splenic artery aneurysm; (2) in kidney (unlikely); (3) in spleen.

Intravenous pyelogram: Control shows large calcified upper abdominal shadow. I.V.P. calcification inconstant in relation to kidney. Kidney function normal, but left slightly displaced downward. Appearance consistent with tuberculoma.

Mantoux (1 : 1,000) strongly positive.

Lieut.-Colonel A. L. Wingfield: The diminution in the size of the spleen from an estimated 6 in. to $2\frac{1}{2}$ in. suggests that the original enlargement may have been due to infarction or thrombosis. The nature of the calcification seems to support this view. The absence of other substantial evidence of tuberculosis also makes tuberculoma an improbable suggestion.

Dr. A. Elkeles: It is doubtful whether the enlargement and calcifications of the spleen in this case are of tuberculous origin. Tuberculous manifestations in the spleen are usually of the miliary type and are the result of hæmatogenous spread. Primary tuberculosis of the spleen is extremely rare. The radiograms of this case reveal two types of calcifications of the spleen, multiple calcifications scattered over the organ and a calcified ring shadow the size of a tangerine near the upper pole. The multiple areas of calcification are not well defined and are mainly of low density, which suggests that the lesions are of more recent origin. Calcified ring shadows of the spleen may be due to a calcified aneurysm of the splenic artery usually showing a double ring shadow with a gap at the

and a third case of complete heart block and patent ductus arteriosus. These cases were similarly investigated with angiocardiograms.

Technique.—The technique used for these films has been that of Robb and Steinberg with certain modifications. After preliminary tests for iodine sensitivity 15 to 20 c.c. of 70% pyelosil are rapidly injected into an arm vein. Films are exposed at injection and at intervals of $1\frac{1}{2}$ sec. for 12 sec., using 8 films in all. The rapid changing of cassettes is facilitated by the cassette-changer shown at the meeting. An exposure of $1/20$ sec. is made using 63 kvp, and 200 ma.

Comment.—Since 1939 when Mr. O. S. Tubbs and myself first embarked on ligation of a patent ductus arteriosus, I have become increasingly aware of the difficulty and importance of accurate diagnosis in acyanotic congenital heart lesions. Now that operation for coarctation of the aorta has been introduced, positive diagnosis of the lesion and exclusion of complicating or compensatory forms of congenital heart disease are even more necessary. The usual methods of clinical and radiological examination are at present unsatisfactory in this respect. The three cases shown at the meeting were selected to illustrate the value of angiocardiography in two instances of patent ductus arteriosus, one with a complicating lesion, one without, and a third case of coarctation of the aorta which is described here.

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(A full account of these and other cases will be published in the *British Journal of Radiology*.)

Mediastinal Tumour.—D. P. F. EMBLETON, M.R.C.S., L.R.C.P. (for N. LLOYD RUSBY, D.M.).

Mrs. E. C., aged 50. Nine months' history of asthmatic attacks, particularly at night. Cough with a little mucoid sputum. Short of breath on exertion. No loss of weight. Exacerbation of symptoms in the autumn. No past illnesses of note.

Florid complexion. No distension of cervical veins. No palpable glands. Dullness

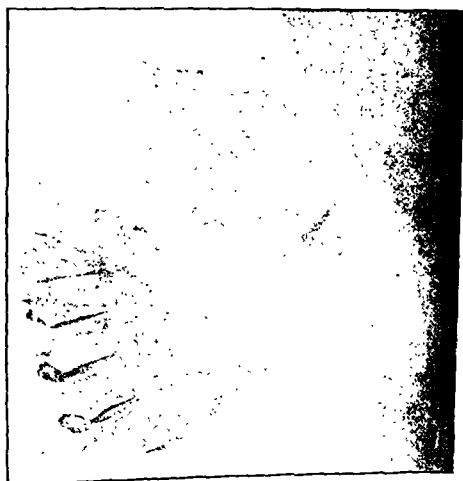


FIG. 1.

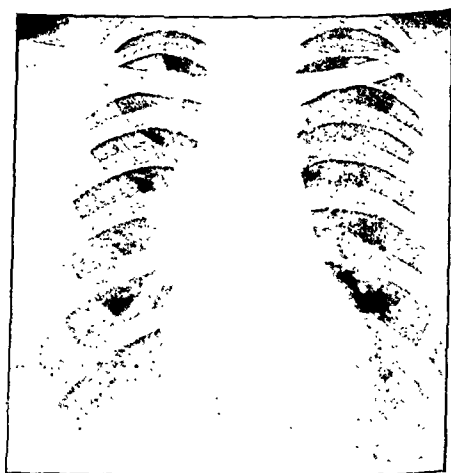


FIG. 2.

to right of upper sternum. Heart N.A.D., B.P. 120/80. R.B.C. 4,480,000. Hb 88%. Sputum: No T.B. Urine N.A.D. Blood Kahn negative. Aschheim-Zondek test negative.

spent in hospital than out, with repeated melæna and hæmatemesis. Barium meals and blood transfusions and œsophageal dilatations punctuated his unhappy existence.

The first operation performed was a phrenic avulsion to relax the crus of the diaphragm, and no benefit resulted. The second was to open the thorax and mobilize the diaphragm into a tent and raise this above the cardia in an endeavour to prevent the loculation of the stomach into acid cardiac and alkaline pylorus portions by the diaphragm. It was noticed that the cardiac orifice was extensively scarred and stenosed, and it was dilated under vision by bougies while the chest was open. After initial improvement from this operation, he soon relapsed into his former condition and continued to deteriorate.

The third operation consisted in a resection of the scarred lower portion of the œsophagus and the cardiac two-thirds of the stomach, the dilated œsophagus was joined end to end to the pyloric third of the stomach; both vagi were of course divided as a result (fig. 2). The result eighteen months later is excellent, weight is nearly doubled, fits have disappeared, anæmia is gone and regurgitation has vanished, so that he now sleeps horizontally in bed. A great mental improvement has resulted from release from all his torments and he is able to make up for the years of education he has lost.

Temporal Arteritis (Giant-Cell Arteritis).—A. P. DICK, M.D.

Male, aged 69. Retired draper.

7.11.47: History of one year's vague aching pains in joints, and of five weeks' dull headache in left temporal region, radiating to vertex and occasionally to left ear and jaw. At same time noticed a "hard vein" in left temple. Previous health good.

On examination.—Frail elderly man. Left temporal artery prominent and did not

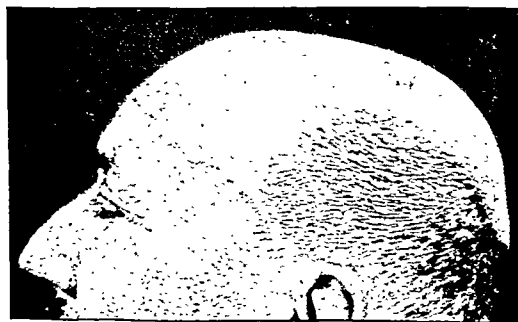


FIG. 1 (7.11.47).—Showing affected temporal artery.



FIG. 2.—Section of artery. ($\times 32$.)

pulsate in distal half; very slight tenderness over proximal part of artery. Right temporal artery also appeared slightly prominent. Blood-pressure 160/90, and evidence of generalized arteriosclerosis and of emphysema but no other abnormal signs. W.B.C. 25,100, polys. 78%. X-ray of skull: Osteoporosis.

origin of the aneurysm. Hydatid and non-parasitic cysts also occur. A case of a large calcified non-parasitic cyst of the spleen confirmed by operation was reported by Elkeles and James (*Brit. J. Radiol.*, 1943, 16, 59), in which displacement of the stomach to the right and downward displacement of the splenic flexure of the colon and of the left kidney were present. The origin of this cyst remained undetermined. Most authors are of the opinion, however, that trauma plays an important part in the development of splenic cysts. Dr. Browning Alexander's patient had an accident in 1940, resulting in fracture of the left lower ribs. It is feasible to assume that at the same time the patient suffered injury to the spleen with subsequent hæmorrhage. Since hæmosiderin predisposes to calcium deposits, it is likely that the multiple calcifications resulted from subcapsular hæmorrhage and the calcified cyst from liquefaction of a hæmatoma.

[March 12, 1948]

Congenital Short Œsophagus.—A. DICKSON WRIGHT, M.S.

C. C., aged 20, was prematurely born and at birth sustained a cephalhæmatoma. His tonsils and adenoids were removed at the age of 2 because of his facies and retarded development. He did not walk until the age of 6 and he was very slow to learn to speak and write.

At about the age of 18 months, epileptic fits were first observed and later it was noticed that these were very often preceded by stomach pains and vomiting. Later in life, vomiting and regurgitation at night became very troublesome, and when he was 13, anæmia became noticeable, and occult blood was present in the stools.



FIG. 1.—Pre-operative condition showed œsophagus with stricture formation.



FIG. 2.—Post-operative condition: pyloric half of stomach completely in chest and pylorus at the level of the cardiac orifice. Œsophagus still remains dilated, but the food passes easily into the stomach.

At the age of 14, an X-ray showed a congenitally short œsophagus which had been missed in previous X-rays. The œsophagus was dilated above a stenosed cardiac orifice, about one-third of the stomach being in the thorax (fig. 1). The lower end of the œsophagus also showed a small ulcer crater. The observation was made at this time that after the stomach had been filled with barium in the standing position, and then the patient lay down, a large amount of the meal refluxed into the œsophagus.

From then on life became progressively more miserable for him. Even with the most carefully chosen food, each meal was a battle, and he could not lie down to sleep, because of the regurgitation. The fits became more frequent. More time was

spent in hospital than out, with repeated melæna and hæmatemesis. Barium meals and blood transfusions and œsophageal dilatations punctuated his unhappy existence.

The first operation performed was a phrenic avulsion to relax the crus of the diaphragm, and no benefit resulted. The second was to open the thorax and mobilize the diaphragm into a tent and raise this above the cardia in an endeavour to prevent the loculation of the stomach into acid cardiac and alkaline pylorus portions by the diaphragm. It was noticed that the cardiac orifice was extensively scarred and stenosed, and it was dilated under vision by bougies while the chest was open. After initial improvement from this operation, he soon relapsed into his former condition and continued to deteriorate.

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Course.—17.11.47: Admitted London Hospital. Now no tenderness over temporal artery. He ran an irregular fever, and repeated blood-counts showed a persistent leucocytosis varying between 15,000 and 22,000 with polymorphs. about 80%. A few days after admission he became progressively more drowsy and disinterested in his surroundings, and slight mental confusion persisted for the next fourteen days. 24.11.47: Lumbar puncture: normal C.S.F. pressure and content. Repeated blood cultures negative; Widal reaction and W.R. negative, and a further lumbar puncture showed no abnormality. Sedimentation rate varied between 25 and 32 mm. in one hour. X-ray of chest clear. 28.11.47: Slight bilateral ptosis and weakness of conjugate upward deviation of the eyes for one day. 1.12.47: Unable to pass water and had to be catheterized for the next eighteen days. Prostate slightly enlarged but soft rubber catheter passed easily. His urine contained a cloud of albumin throughout. Blood urea 63 mg.%. Treated empirically with 30,000 units intramuscular penicillin three-hourly from December 2 to 18. By 8.12.47 had become less drowsy and confused. 10.12.47: Biopsy performed on left temporal artery.

Microscopic examination.—Degeneration of media with some infiltration with round cells and plasma cells, infiltration of the adventitia with round cells and a ring of giant cells in the outer part of the media. Gross hypertrophy of the intima almost occluding the lumen.

Following the biopsy he ceased to complain of headache and after 25.12.47 he had only slight occasional fever. His general condition improved gradually. 8.1.48: Discharged. 5.3.48: Again complaining of slight headache in left temporal region for few weeks. W.B.C. 8,300, polymorphs. 80%. E.S.R. 20 mm. in one hour.

Comment.—This condition, which is characterized by an inflammation of segments of arteries, with thrombosis, is probably much less rare than the reported cases, less than 50, would suggest. Its curious predilection for the temporal arteries is by no means constant, and a number of cases have now been reported in which the scalp vessels have not been affected. In the absence of involvement of the scalp or retinal arteries, or of a limb artery, the clinical picture may be obscure, and it may present as a long-continued illness in elderly people, with pyrexia, and at times with cerebral complications. There was no clinical evidence of involvement of other arteries in this case, apart from his mental state and the transient ptosis which suggested that some intracranial vessels were involved.

The microscopical picture in this patient was typical of giant-cell arteritis. His improvement following the biopsy is in accordance with most previously recorded cases. The case is of interest in that the very high leucocytosis (24,000) led to the suspicion of a concealed pyogenic infection as the cause of his illness. A slight leucocytosis is the rule in this condition, and the highest figure previously recorded is 17,000 (Sproul, 1942). There is one report by Robertson (1947) of a patient with this condition being treated with penicillin, which, as in this case, had no noticeable effect. The case was also unusual in that there was only slight tenderness over the affected artery and apart from the evidence of obstruction in its distal portion, there was little difference between the temporal vessels on each side.

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- ROBERTSON, K. (1947) *Brit. med. J.* (ii), 168.
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Section of Orthopædics

President—V. H. ELLIS, F.R.C.S.

[November 4, 1947, concluded]

Invalid Chair.—J. E. GULL (*Research Fellow in Orthopædic Appliances to the British Orthopædic Association*).

The function of this chair is to raise the occupant from a sitting to a standing position (see fig. 1).

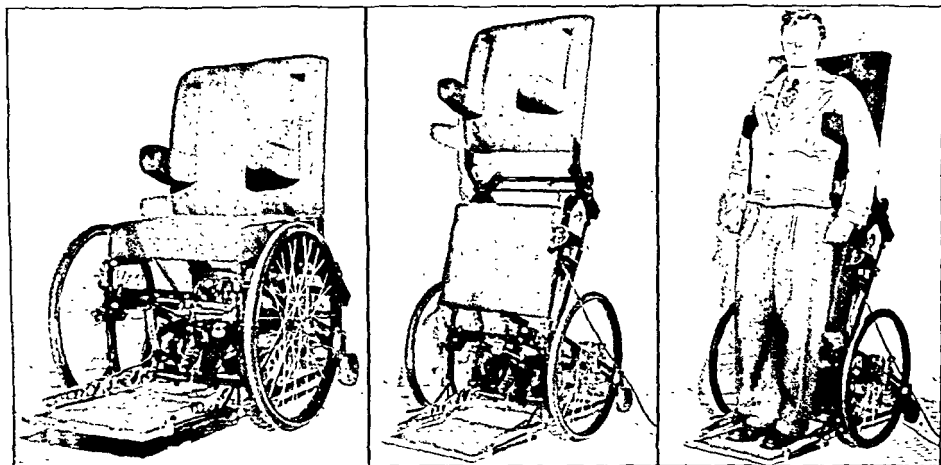


FIG. 1.—Invalid chair designed by J. E. Gull. Latest developments include arm-rests adjustable for width, back adjustable for angle, and complete arm-chair comfort.

It was originally designed for a friend who had been totally incapable of getting out of a chair unaided since an attack of infantile paralysis eighteen years ago, yet who, when once standing up, can walk. This chair enables her to get up entirely by herself without difficulty. It would, no doubt, be of equal value in cases of paralysis, arthritis, or, in fact, any complaint which makes it difficult or impossible to get up from a chair, and is likely to make all the difference in life to those who need it.

Power is supplied from the electric mains with one 3-way switch operated by the occupant—"Up", "Off" and "Down". The machine stops itself automatically at each end of its travel.

Suitable lengths of flex are provided for attachment to light or power points, and the free end of each can be plugged into the chair socket by the occupant.

The chair is fully adjustable for height to suit individual requirements. The foot-rest is raised and lowered automatically and is adjustable for height; this also prevents the chair from moving when operated on a slope.

[December 2, 1947]

Chondroma of the First Metatarsal Bone.—DAVID TREVOR, M.S.

E. B., male, aged 36.

History.—First seen on November 4, 1946, when patient stated that he had noticed a hard swelling on the inner side of the right foot for the last three weeks.

Examination revealed a hard, painless swelling which extended across the plantar and dorsal surfaces of the foot below and above the second metatarsal bone. X-rays showed gross expansion of the first metatarsal of the right foot with thinning of the cortex and appearance of fibrocystic disease of the medulla (fig. 1).

At operation the first metatarsal bone was excised except for the head. A bone

Course.—17.11.47: Admitted London Hospital. Now no tenderness over temporal artery. He ran an irregular fever, and repeated blood-counts showed a persistent leucocytosis varying between 15,000 and 22,000 with polymorphs. about 80%. A few days after admission he became progressively more drowsy and disinterested in his surroundings, and slight mental confusion persisted for the next fourteen days. 24.11.47: Lumbar puncture: normal C.S.F. pressure and content. Repeated blood cultures negative; Widal reaction and W.R. negative, and a further lumbar puncture showed no abnormality. Sedimentation rate varied between 25 and 32 mm. in one hour. X-ray of chest clear. 28.11.47: Slight bilateral ptosis and weakness of conjugate upward deviation of the eyes for one day. 1.12.47: Unable to pass water and had to be catheterized for the next eighteen days. Prostate slightly enlarged but soft rubber catheter passed easily. His urine contained a cloud of albumin throughout. Blood urea 63 mg.%. Treated empirically with 30,000 units intramuscular penicillin three-hourly from December 2 to 18. By 8.12.47 had become less drowsy and confused. 10.12.47: Biopsy performed on left temporal artery.

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Comment.—This condition, which is characterized by an inflammation of segments of arteries, with thrombosis, is probably much less rare than the reported cases, less than 50, would suggest. Its curious predilection for the temporal arteries is by no means constant, and a number of cases have now been reported in which the scalp vessels have not been affected. In the absence of involvement of the scalp or retinal arteries, or of a limb artery, the clinical picture may be obscure, and it may present as a long-continued illness in elderly people, with pyrexia, and at times with cerebral complications. There was no clinical evidence of involvement of other arteries in this case, apart from his mental state and the transient ptosis which suggested that some intracranial vessels were involved.

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- ROBERTSON, K. (1947) *Brit. med. J.* (ii), 168.
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Five weeks later the plaster-of-Paris cast was removed. The wounds were found to be soundly healed, and it appeared the graft had taken. Her progress was then satisfactory and showed steady improvement.

She stated she had been back at work since June of this year, and had been minding a machine since then. She could use her hand for almost everything she wanted to do.

She is now awaiting operation for repair of the long extensor tendon of the thumb.

Larsen-Johansson's Disease.—GEORGE BONNEY, F.R.C.S. (for DAVID TREVOR, M.S.).

P. S., male, aged 11.

History of aching pain in both knees, worse on the left side, for the past eighteen months. Relieved by rest and made worse by exertion. Pain was bad during the winter of last year when he was playing a lot of football, was almost absent during the summer and recurred when he started playing football again this year.

Past and family history.—Nothing relevant.

Physical signs.—Tenderness of lower pole of the patella, more marked on the left side, with slight swelling in this site. No limitation of knee movements.



FIG. 1.
Right knee.

On first attendance, 26.11.47.



FIG. 2.
Left knee.

On first attendance, 26.11.47.



FIG. 3.
Right knee (25.2.48) after 8 weeks' immobilization in plaster.

X-rays show: Accessory centre of ossification at lower pole of patella; fragmentation of tibial tubercle apophysis, rather similar to changes in Schlatter's disease (figs. 1 and 2). Fig. 3 shows fusion of inferior patellar ossicle (R. knee) to rest of patella, after eight weeks' plaster immobilization.

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Synovioma of Right Ankle Region.—A. W. LIPMANN KESSEL, M.C., M.B.E., F.R.C.S. (for V. H. ELLIS, F.R.C.S.).

Miss E. S., aged 38.

History of painful swelling of right ankle-joint for two months.

She gave a history of having sprained her right ankle while in the A.T.S. in 1942.

graft from the fibula of the same leg was inserted (fig. 2) and the foot immobilized in a plaster-of-Paris cast for ten weeks.

Histological section of the tumour removed showed it to be a pure chondroma with large areas of myxoid degeneration.

Comment.—The patient has made satisfactory progress and, a year after operation, he has full range of movement of his foot without any complaint whatever; he has been back at work for many months and now states that he is able to play football as well as before (see fig. 3).



FIG. 1.



FIG. 2.



FIG. 3.

FIG. 1.—Chondroma of first metatarsal, simulating X-ray appearance of fibrocystic disease; anteroposterior view.

FIG. 2.—Excision of first metatarsal, leaving the head. Bone graft from fibula placed between head and internal cuneiform.

FIG. 3.—Ten months after bone-grafting operation. The graft has become hypertrophied and has assumed more closely the shape of the first metatarsal bone.

Compound Fracture of the Radius and Ulna with Division of Dorsal Structures of Wrist-joints.—DAVID TREVOR, M.S.

D. S., aged 42. Admitted to hospital 11.11.46.

History of having caught her right forearm and hand in a machine while at work. On examination she was found to have a skin wound completely encircling the forearm, just above the wrist-joint. There was comminution of the lower end of the radius, a fracture dislocation of the lower end of the ulna, the proximal carpal joints were opened, all extensor tendons were severed, the flexor carpi ulnaris tendon was severed, the medial nerve was intact, the ulnar nerve was also intact, the radial nerve was severed at the wrist, but the bulk of the flexor tendons were intact.

At operation the same day the lower ends of the radius and ulna were brought together. Some dead muscle was excised and the skin sutured. Plaster of Paris was applied.

On 21.11.46 the fracture was manipulated, and re-manipulated on December 9. The position was then found to be fairly good and the wound had healed by first intention.

On 27.1.47 a free tendon graft was taken from the tendon of palmaris longus, and this was inserted between the cut ends of the extensor tendons. $1\frac{1}{2}$ in. of the lower end of the ulna was excised at the same time. The wound was closed and plaster of Paris applied.

When admitted to hospital about six weeks after her first attendance at the Out-Patient Department, pulsation of the tumour became evident.

Subsequent X-rays revealed a progressively destructive lesion in the region of the lateral malleolus as well as rapidly increasing general decalcification (figs. 1A and B and 2A and B).

A below-knee amputation was carried out, and the pathological report established the diagnosis that the tumour was a synovioma.

The most recent chest X-ray (January 1948) shows opacities very suggestive of early metastatic tumour deposits.



FIG. 3.

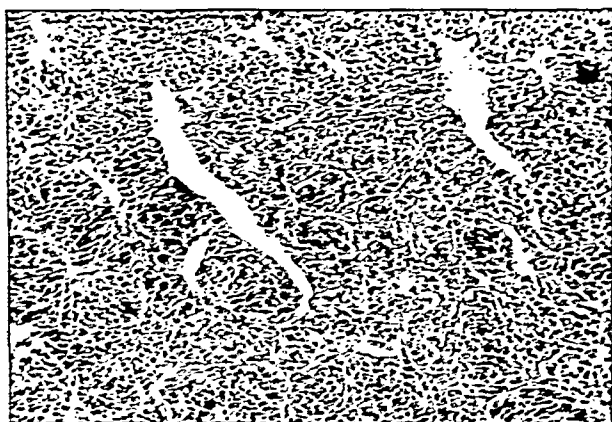


FIG. 4A. $\times 124$.

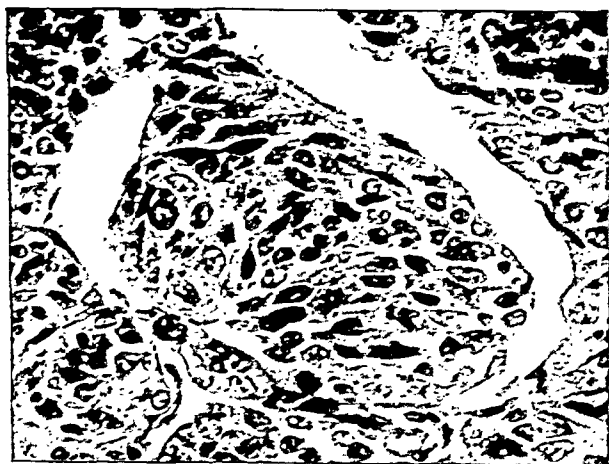


FIG. 4B. $\times 477$.

Pathology (Dr. R. H. Hepinstall).—The specimen (fig. 3) shows a soft friable tumour mass, mainly white in colour but with numerous hæmorrhagic areas, invading the lateral malleolus, talus and calcaneus. The latter is completely filled with growth and the bone is thinned and deficient in places. There is a close relationship between the tumour and the peroneal tendon sheaths, suggesting a possible site of origin.

Microscopically the main part of the tumour consists of spindle-shaped cells with scanty stroma, within which are clefts and larger spaces lined by tumour

This was treated by some form of injection (presumably novocain, but no details have been traceable). She was fit for duty after one week and had no further trouble apart from occasional twinges in her ankle, until June 1947, when she again twisted her ankle. She was treated by her own doctor with ointments and massage for a sprained ankle. Since that time pain has persisted and swelling of the ankle has gradually increased. There was no noticeable loss of weight or impairment of general health.

On examination.—Healthy-looking young woman. General examination revealed no significant abnormality. R. ankle: Irregular, soft, doughy mass about 4 in. in diameter and occupying the whole of the external malleolar area. The malleolus itself is not palpable. Definite pulsation can be elicited but there is no bruit audible on auscultation and the mass cannot be emptied by pressure.



FIG. 1A. 23.9.47.



FIG. 1B. 23.9.47.

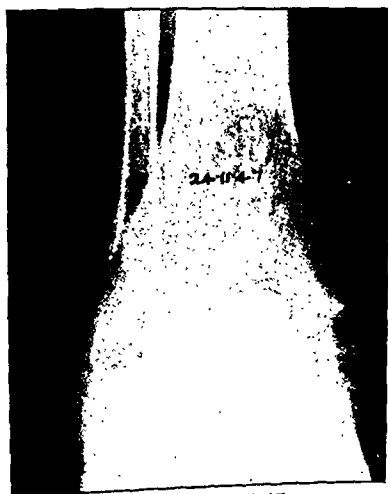


FIG. 2A. 24.11.47.



FIG. 2B. 24.11.47.

Discussion.—When first seen, the swelling appeared to be confined to the peroneal tendon sheaths. An X-ray showed some general osteoporosis, more marked in the external malleolar area. The provisional diagnosis of tuberculous tenosynovitis was made with some confidence. However, investigations (X-ray chest: No evidence of T.B., Mantoux 1 : 1,000 negative, and E.S.R. 10 mm./hr.) were all against this diagnosis.

Costo-clavicular Compression Following Fracture of Clavicle.—J. S. BATCHELOR, F.R.C.S.

This patient, a woman aged 38, sustained a fracture of the left clavicle in June 1946 and ever since this injury has complained of pain in the shoulder radiating down the arm into the ulnar border of the forearm and hand.

Examination shows malunion of the fracture with considerable dropping of the shoulder-girdle (fig. 1). There is wasting of all the muscles of the left arm, the hand



FIG. 1.

is cold and the left radial pulse is diminished in volume compared with the right. Symptoms appear to be due to costo-clavicular compression as a result of malunion of the fracture.

Congenital Dislocation of the Shoulder.—E. HENRIETTA JEBENS, F.R.C.S.

I. B., a girl aged 16.

Complaint.—Inability to put her right hand behind her head, to her mouth or behind her back. Unable to lift anything heavy.



FIG. 1.

FIG. 2.

History.—Forceps delivery, but no signs of trauma to the child. A few days after

certain areas there are cell tufts containing polygonal cells, which show a tendency to grow into the clefts. Mitotic figures are numerous. The appearance is that of a highly malignant tumour of synovial cell origin (figs. 4A and B).

Bilateral Bony Ankylosis of Hip-joints.—F. A. SIMMONDS, F.R.C.S.

A. B., male, aged 20.

History.—Eight years ago acute osteomyelitis of the pelvis, resulting in solid bony fusion of both hips.

The left hip became fixed in 10 degrees adduction; neutral rotation; 20 degrees flexion.

The right hip fused in the position of 20 degrees abduction; 40 degrees external rotation; 50 degrees flexion.

The boy can now walk five miles, dance, and run up and down stairs easily. He is able to sit or stand for long periods without discomfort.

The spine and knees are strong and mobile and it is realized that such conditions are ideal for function, but it is felt that this function is better than it would have been had Nature fused his hips in the more usual position with the legs parallel.

Are we right in accepting this parallel position? Would it not give better function and split the load on the back, to have one hip flexed 20 degrees and the other 40 or 50 degrees, in conditions where it is apparent that both hips will become ankylosed.



Spontaneous Fracture of a Metacarpal.—

C. HOPE CARLTON, M.C., M.Ch.

The patient, a male aged 35, is a porter at Euston. On November 2, 1947, he was lifting a parcel weighing 30 lb. on to the rack of a railway compartment. He heard a crack and felt a pain in his hand.

X-ray examination shows an oblique fracture of the fourth metacarpal bone (*see fig.*).

He has made a normal recovery. The case is shown as the patient is certain that he did not knock his hand on the rack nor did the parcel hit it. There was no direct violence, it was spontaneous.

The patient's blood phosphorus is double the normal and his blood calcium half the normal. He appears to be in the best of health and has had no bony lesion in his life apart from this one.

Operative Prevention of Myositis Ossificans.—W. H. GERVIS, F.R.C.S.

Male, aged 28.

History.—26.12.46: Had a blow on the right thigh at football.

First seen 3.1.47. Very large hæmatoma under the right quadriceps, the type that progresses to myositis ossificans.

Operation (5.1.47).—Lateral incision and evacuation of hæmatoma.

X-ray (31.1.47) showed very slight myositis ossificans only.

Left hospital 12.2.47. Returned to full work 12.4.47.

Condition now: Full range of movement of knee; quadriceps normal.

(c) It would stimulate growth of the joint in general and of the margins of the acetabulum in particular.

(d) It would increase muscular strength and give normal muscle balance.

(e) It would allow the child to get about and so avoid the psychological damage of long and uncomfortable immobilization in plaster.

(f) It would make things much easier for both parents and surgeon.

(4) The head can only leave the acetabulum backwards. Owing to the action of the ilio-femoral band it can only go backwards if the knee goes forwards. Therefore any movement is permissible as long as the knee is kept back.

(5) The ilio-femoral band or ligament of Bigelow is the most important factor in this condition for four reasons.

(a) It is upon the fulcrum supplied by it that the head is levered into position in the usual methods of reduction. This means that the force used in pressing the knee back is multiplied about eight times in pressing the head against the rim of the acetabulum, with consequent risk of damage.

(b) The head will slip in most easily if this ligament is relaxed, as it is in the foetal position of the limb.

(c) In older cases in which reduction by manipulation is impossible, this ligament is the obstacle, and if divided the head may be pushed into place in the way described.

(d) In unreduced cases the pain and instability of the limb are mainly due to the head of the femur swinging over a wide area on the fulcrum of this ligament. Division of it may allow a stable false joint to be formed.

APPLICATION OF THE HYPOTHESES

Reduction of the deformity.—The child is laid on its face, and the dislocated thigh brought into the "foetal angle".



FIG. 1.

Through the heel of one hand, the surgeon transmits his weight with a stiff arm on to the great trochanter, while with the other he moves the knee up and down through a small angle. When the exact point of entry is reached the head should go in with a characteristic crunching feeling, often divided into two stages. The commonest error is to mistake a movement of the head forward above the trochanter for a reduction. If this occurs the head will be felt to rise and fall when the knee is moved up and down, whereas in a true reduction no movement can be detected under the palpating thumb (fig. 1).

Plastering after reduction.—To allow reactions to settle down and the muscles adjust themselves to the new position of the bones it is necessary to leave the hips in a double spica for a month. The hip is left unmoved once it is in: the temptation to demonstrate the reduction by snapping it in and out must be resisted. The child is raised face downwards by an assistant on either side grasping the legs below the knee and so raising the pelvis off the table while maintaining the utmost abduction of the thighs possible. The plaster should be strengthened by a slab over the back and junctions of the body and thighs, and should leave as wide a "nursing area" round the perineum as possible. The knee on the side of a dislocation should be included, as otherwise some degree of adduction is possible.

birth an abnormality of the right shoulder was noticed and the child taken to Guy's Hospital. Treated on an abduction splint for a few weeks.

Family.—The patient is the youngest of seven children. The father and three brothers have severe deformities of hands and feet.

On examination.—The patient holds her right arm internally rotated and slightly abducted. There is limitation of external and internal rotation and extension of the right shoulder-joint. Right elbow shows slight limitation of extension. Wrist and hand normal and grip equal to left. Wasting of right deltoid, arm and forearm muscles, but no paralysis and electrical muscle tests are all normal. Right scapula higher than left and slightly smaller. There is a subspinous dislocation of the humeral head.

X-ray: There is a backward dislocation of a deformed humeral head. The acromion process is arched downwards and the coracoid process greatly elongated (fig. 1). A rudimentary glenoid only is present and the humeral head appears to articulate with its posterior border. Upper one-third of shaft of humerus curved with convexity forwards (fig. 2—X-ray taken through joint from above downwards).

Comment.—Since R. W. Smith first recorded congenital dislocations of the shoulder-joint in 1839 21 cases, of which 8 were bilateral, have been reported in the literature. Grieg, reviewing all reported cases of shoulder dislocations in infants, in 1923 came to the conclusion that there were 3 types: viz. true congenital; obstetric; paralytic. At that date he found 10 cases of undoubted primary congenital dislocations of the shoulder of which 2 were bilateral. Since that date 11 cases (excluding the one I have now described), of which 6 were bilateral, have been reported. Scudder described 2 cases in one family and Valentin 3 members of one family with this deformity. Wolff describes a bilateral case; the grandfather, mother and one uncle of this patient had severe congenital deformities of the hands closely resembling my case. In a number of the reported cases other congenital deformities were associated with the shoulder dislocation.

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This meeting will be continued in the next issue of Orthopædics Section and will contain Mr. F. P. FitzGerald's case of "Leadbetter's Osteotomy" and Dr. T. M. Robb's "Tumour of Femur."

[February 3, 1948]

The Treatment of Congenital Dislocation of the Hip

By DENIS BROWNE, F.R.C.S.

HYPOTHESES UPON WHICH THIS TREATMENT IS FOUNDED

- (1) THE hip is dislocated during intra-uterine life by a thrust upon the knee from the uterine wall sending the head of the femur backwards out of the acetabulum.
- (2) In consequence the best way to get the head back into place is to reverse the process, and with the shaft of the femur held in the same direction as when dislocation occurred, to thrust it upward and forward by pressure on the great trochanter.
- (3) Active movement of the femur, when the head is in position would have six good effects:
 - (a) It would cause atrophy by pressure of any tissues lying between the cartilage of the head and that of the acetabulum.
 - (b) It would have a "self-centring" action, which would work the head into the true centre of the socket.

Film: Curare (Intercostrin) in the Treatment of Acute Anterior Poliomyelitis

Commentary by Sir REGINALD WATSON-JONES, F.R.C.S.

A FILM by Dr. Nicholas S. Ransohoff of New York, which had been brought to this country by Sir Morton Smart, was introduced by Sir Reginald Watson-Jones. Dr. Ransohoff accepted the evidence of Plato-Schwartz that in acute anterior poliomyelitis there was widespread muscle spasm, and he believed that such spasm was responsible for dysphagia, respiratory embarrassment and early onset of deformity. By injection of curare the spasm was relieved, Sherrington's law of reciprocal innervation was re-established and the pathological stretch reflex was obliterated. The dosage employed was 0.9 unit per kilo of body-weight every eight hours for the first twenty-four hours; the dosage thereafter being increased, if there was no adverse reaction, to 1.5 units per kilo of body-weight every eight hours. Intramuscular injection was continued until all evidence of muscle spasm had disappeared.

The essential principle of Ransohoff's treatment was not simply to give curare injections, but to make use of such injections in order to institute passive stretching, exercises, weight-bearing and ambulation at the earliest possible moment. The exercises and movements were started within twenty-four hours of admission. At three separate intervals during the first three hours after each daytime dose of curare, every joint of the body was put through as complete a range of movement as possible. All muscles of the extremities, back and neck, were stretched in the attempt to re-establish normal muscle length. The patient was put on his feet as early as possible, no attempt being made to avoid physical tiredness or fatigue. Throughout the hours that joints and muscles were not being stretched the patient exercised with parallel bars, specially constructed chairs, trapeze fastened to the foot of the bed, mariner's wheels, bicycles, and every type of occupational therapy apparatus. The patients were kept busy continuously.

It was emphasized that no claim was made to have established a cure for anterior poliomyelitis, but it was believed that this treatment gave better results more quickly than by any other method. In a series of 29 patients, no fixed deformities or contractures developed. 5 patients with bulbar paralysis responded in a surprising manner to adequate doses of curare, the relief being attributed to relaxation of spasm of the accessory muscles of respiration and of the diaphragm. Dysphagia responded immediately and dramatically.

Sir Reginald Watson-Jones said that although he had introduced the film it must not be thought that he accepted Ransohoff's principles. He quoted the words of Voltaire: "I utterly disagree with what you say, but I would defend to the death your right to say it". He thought that further electromyographic investigation was needed into the question of spasm in poliomyelitis and the extent to which spasm, if it existed, was an important factor calling for special treatment. Further evidence was needed before it could be accepted that treatment by the injection of curare altered the prognosis and improved the outlook. That part of Ransohoff's treatment which insisted upon early mobilization and weight-bearing, passive stretching despite pain, and exercise despite fatigue, was in startling contrast to the principles advocated by Hugh Owen Thomas and Robert Jones. It might be that in the past we had over-emphasized the importance of protecting paralysed muscles. It might be that avoidable joint stiffness had sometimes been allowed to develop. It was possible that earlier mobilization and ambulation were advisable. But he would need much more than the evidence of this film to persuade him that fatigue and exhaustion of weak and partly paralysed muscles were desirable. Still more did he feel revulsion, amounting almost to horror, when he saw painful joints and muscles being stretched and forced despite the shouts and screams of the patient.

Maintenance of active movement within the limits laid down.—This can be managed by the device illustrated, consisting of a bar connecting two rings which encircle the thighs, and which is held against the abdomen or the small of the back by a soft belt to which it is sewn. The anterior position is the more comfortable, but the posterior gives greater abduction (fig. 2).

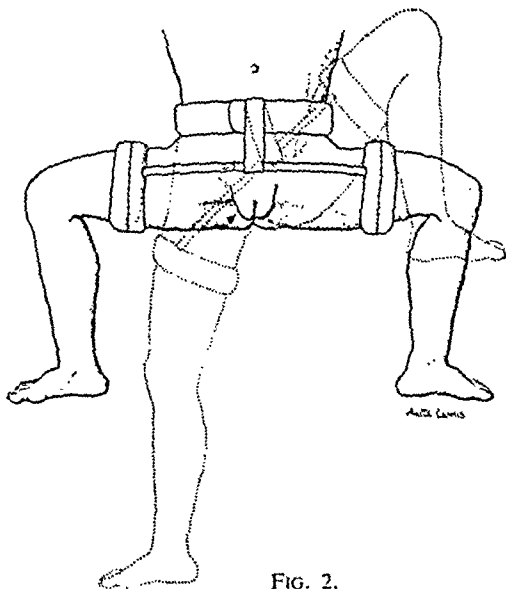


FIG. 2.

In this apparatus the child is allowed complete freedom to get about as it wishes. There are three main ways of progression. The first is on hands and feet, the second in the position of a Cossack dancer, with the knees bent and the buttocks near the floor, and the third is a semi-erect position with the knees widely separated.

The movement that looks most alarming, that of bringing the one leg down till the child stands upright on it, has three safeguards:

- (a) It can only bring the leg down while the other one is pointed up, with a consequent tilting of the pelvis which means that extension is much less than it seems.
- (b) This position is only possible with a strong contraction of the gluteus maximus, which pulls the great trochanter backwards and so keeps the head forwards.
- (c) The child will not put this heavy strain on the hip-joint unless it is stable; the Trendelenburg test on an unstable hip is obviously most uncomfortable.

Indications for removing apparatus.—These turn on the X-ray appearances, the willingness of the child to stand on the joint in the Trendelenburg test position, and the strength of the muscles. As a general guide it may be said that about nine months in the apparatus is an average. The children are so contented in it that there is no hurry about releasing them. When the surgeon decides the hip is stable he takes off the apparatus and allows the child to do what it will. In about three months it is walking normally.

Difficulties and setbacks.—If the hip slips out in the early stages, either in plaster or the apparatus, the treatment is simply begun again. In difficult cases one should not be afraid of forcing the knee back till it is behind the pelvis.

Results.—In the 42 cases I have treated by this method, all of them under 4 years of age, I have in all obtained stable painless hips. Some of them have slipped out once or more in the early stages but setbacks of this kind do not seem to spoil the final result. Many of the mothers report that their children "run faster than any of the other little girls".

Warning.—The apparatus described is quite unsuitable for cases that have not been reduced and plastered in the way described.

OPEN OPERATIONS.—I have tried in three older irreducible cases the division of the ilio-femoral band followed by treatment upon the lines described. The number is far too few upon which to form an opinion, but the results have been very encouraging.

REDUCTION OF AN ADULT TRAUMATIC CASE.—Without drawing any conclusions I would record that a posterior dislocation in an adult male following a railway accident was reduced with ease and speed by an intelligent but inexperienced house surgeon using the method described.

I should like to acknowledge the stimulation I have received in this work from the writings and conversation of Dr. F. Bauer (1936, *Lancet* (i), 1057).

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Hallux Valgus in the Adolescent

By A. ROCYN JONES, F.R.C.S.

HALLUX VALGUS is a disability that may reveal itself in early adolescence and it occurs almost invariably in females. As in the adult, the severity of the malady varies a great deal but great abduction of the big toe and a prominent bunion may occur in a patient even at 12 years of age. In the deviation of the toe the shoe plays a secondary part; many of these girls have worn footwear of good shape. The primary deforming cause is the adduction of the first metatarsal, the greater the adduction of this bone the greater the abduction of the phalanx. That a deformity of considerable severity may occur concurrently with the quickening growth of the foot in early adolescence may be due to the presence of an adduction of the metatarsal at birth which remained concealed in the smaller undeveloped foot of the young child. It is only with the greater growth of the metatarsal that the deforming influence of the shoe upon the toe becomes operative. And many patients complaining of the symptoms of hallux valgus in adult life probably derive the disability through a congenital adduction of the first metatarsal. Indeed some of these older patients declare that the deflection of the great toe and discomfort dated from their youth. It is possible that this particular metatarsal adduction is atavistic, having some morphological reference to the prehensile great toe of the higher primates.

Most of these patients are brought for advice because of pain in the great toe due to pressure on the head of the metatarsal. It is advisable to have a radiograph taken in order to determine the degree of metatarsal adduction, the amount of separation between the heads of the first and second metatarsals and the extent of the subluxation of the first phalanx if any. In the lesser degrees of adduction relief can be obtained by gentle stretching of the great toe, exercises, and splinting at night. If these measures fail then the prominence, or so-called exostosis, should be removed. In the severely adducted metatarsal, however, this procedure is not enough. But a reconstruction of the joint should not be attempted, because interference with the first phalanx is likely to damage or destroy the epiphysis, and removal of the head of the metatarsal will result in a shortened shaft with loss of effective thrust and weight-bearing by the great toe. An osteotomy of the shaft of the metatarsal in its proximal half is the better procedure and it should take the form of a modified cuneiform osteotomy whereby only part of the wedge is removed and the rest left as a spike to be impacted into the proximal segment. This device secures complete stability of the broken fragments whilst at the same time enabling angulation to take place as a means of correction of the adduction. Simple osteotomy alone is an uncertain corrective because the fragments are unstable and angulation difficult to maintain. After operation a plaster-of-Paris cast is applied from the upper calf to the ends of the toes. Gentle pressure outwards and slightly downwards on the first metatarsal head is exerted until the cast is set. The plaster is retained for six weeks after which the patient is taught exercises and mild stretching of the great toe.

The operation has only been performed where there was persistent pain whilst wearing a shoe and in every case complete relief has followed operation. It is mainly suitable for the severe type of hallux valgus where there is considerable adduction of the first metatarsal; the angulation of the fragment after osteotomy is then easier and more effective; the subluxation of the phalanx becomes automatically corrected. The great advantage in the adolescent is that the operation is entirely extra-articular. It is also applicable to adults although it has only been tried in those under 40. Older patients do not take kindly to the suggestion of having the foot for six weeks in plaster of Paris as compared with the shorter period of inactivity following reconstruction of the joint. The convalescence, however, is shorter and more comfortable after osteotomy and the joint movement is unrestricted.

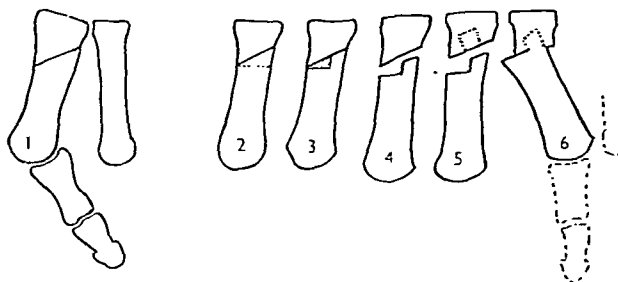
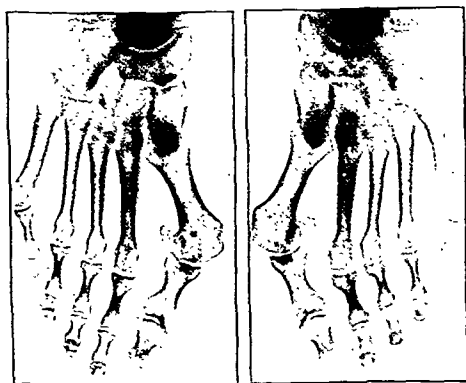


FIG. 1.—A diagram indicating the steps in the operation of oblique osteotomy with impaction for the correction of severe painful hallux valgus in the adolescent. The first metatarsal is exposed in its whole length through a dorsal longitudinal incision in the skin. (1) Site and direction of osteotomy. (2) Wedge of bone required to be obliterated to produce correction of the adduction. (3) Shaded triangular area is the amount of bone actually removed by bone-cutting forceps. (4) "Spike" formed on distal segment. (5) Dotted area represents the medulla which should be broken, but not removed, by a narrow osteotome. (6) Impaction of spike into proximal segment and angulation of fragments.



R.

L.

FIG. 2.—A. S., a young adult, a radiograph of whose feet shows all the signs of a severe bilateral hallux valgus. Note the adduction of the first metatarsal, the wide space between the first and second metatarsal heads and the subluxation outwards of the proximal phalanx.



R.

L.

FIG. 3.—A. S., after the operation of oblique osteotomy with impaction. Note the correction of the adduction of the first metatarsal; the reduction of the subluxation of the phalanx; and the narrowing of the anterior half of the metatarsus as compared with fig. 2.

Cup Arthroplasty of the Hip, with Film

By G. K. McKEE, F.R.C.S.

A SERIES of 10 cases of cup arthroplasty were shown together with a film illustrating the results in four of them, and the methods employed in giving active exercises following on the lines adopted by Smith-Petersen.

The operation of cup arthroplasty is indicated in degenerative conditions of the hip-joint, particularly if bilateral, but it is important that the patients should be capable of performing vigorous physical exercises afterwards, if the best results are to be obtained.

The 2 failures.—3 cases of aseptic necrosis of the head of the femur are included, 1 a success, and the other 2 failures. The successful case is shown in some detail in the film. There is no doubt about the necrosis of the head of the femur, it arose following a dislocation. The necrosis did not involve the whole of the head, however, but only the peripheral portion. At operation, there was plenty of good healthy bone left after removing the degenerated portion. The 2 cases of aseptic necrosis where the operation of cup arthroplasty failed were sequelæ of fractures of the neck of the femur, and practically the whole head had to be removed at operation, before good bone was obtained.

Aseptic necrosis, following a fracture of the neck of the femur, is still one of the unsolved problems of orthopædic surgery. Where there is extensive degeneration of the head of the femur, a cup arthroplasty is not a satisfactory solution.

The other 8 cases.—The film shows 4 of the patients, the 3 excellent results, and 1 of the good results.

There were 4 other good results, in which the range of hip movement had been increased, the patients' activities increased, and the symptoms lessened (*see table*). In the film the patients can be seen exercising after operation, with rollers attached to their heels, running on inclined boards, so as to facilitate abduction movements in the recumbent position. The progress was followed up at intervals, and such acts as sitting, doing up their boots, cycling, walking, and even running, were gradually obtained.

The inadequacy of modern procedures.—The Whitman or Colonna reconstruction operations have never been very popular in this country, and lately the use of a metal cup, to cover the stump of the neck after removal of the great trochanter, in the Whitman type of operation, or to cover the trochanter itself in the Colonna procedure, has been tried in America, and may be useful under special circumstances, but I have no experience of them.

A subtrochanteric osteotomy of the MacMurray type, or an osteotomy combined with an attempt to obtain ischio-femoral osteosynthesis (Brittain's operation) are often employed, but obviously have many major disadvantages, of which the encasement of the patient in an enormous plaster is not the least.

Mr. McKee went on to describe a model which had been made in brass of an artificial hip-joint. This has not yet been used on a human being. It is designed to adjust itself for changes in rake and length.

The model should be made up in vitallium before trying it on the human body.

CUP ARTHROPLASTY RESULTS

Result		Indication for operation
Excellent	3 cases	2 cases of osteo-arthritis 1 case of aseptic necrosis of the femoral head
Good	5 cases	All cases of osteo-arthritis
Failures	2 cases	Both cases of aseptic necrosis

Section of Physical Medicine

President—W. S. TEGNER, M.R.C.P.

[March 10, 1948]

The Role of Physiotherapy in the Treatment of Poliomyelitis

By F. S. COOKSEY, O.B.E., M.D.

PHYSIOTHERAPY plays a large part in the treatment of poliomyelitis and it is expedient to review the subject after the epidemic of 1947. There are few disorders more distressing than the severe manifestations of this disease with its predilection for the younger members of the community and the extreme helplessness it may leave in its wake.

As yet there is no specific prophylactic or cure for the disease. It is not surprising therefore that promising new methods of treatment are tried sometimes with the haste which leads to exaggerated claims. We have so much to do with these patients during the stage of potential recovery that it is our special duty to maintain a critical judgment. We must sustain the confidence of patients and relatives throughout a long period of potential improvement and at the same time avoid raising false hope.

I support Seddon's view that it cannot be too strongly emphasized that no one has ever cured a case of poliomyelitis. All that we can do is to help or hinder a process of recovery that is quite outside our control (Seddon, 1947). Seddon is referring to the treatment of the disease after the virus has invaded the central nervous system. This does not preclude the possibility that future means will be found to induce immunity or arrest the activity of the virus before irreparable damage has been done. Nevertheless it is highly probable that such an advance, when it comes, will be in the laboratory. New forms of physiotherapy must be presumed to be potential weapons to assist recovery and not the means to prevent or cure the disease. At the same time we must remember that we can help Nature to localize and destroy the virus by such means as rest and heat, which is every bit as important as preventing deformity and assisting recovery of function.

We are prone to accept the diagnosis of poliomyelitis too easily. McAlpine and his colleagues investigated 104 cases admitted between August and October last year to a unit for the early treatment of poliomyelitis at the Middlesex Hospital. They arrived at the following classification:

(1) Non-paralytic poliomyelitis 24 cases; (2) paralytic poliomyelitis 26; (3) polio-encephalitis 4; (4) abortive poliomyelitis 6; (5) incorrect diagnosis 44 cases.

Thus of 104 cases admitted with a tentative diagnosis of poliomyelitis only 26 proved to have the paralytic form of the disease, although other cases showed transient paresis which cleared up spontaneously in a short time (McAlpine, Kramer, Buxton and Cowan, 1947). It is obvious that if these cases had come under the care of less critical clinicians quite erroneous conclusions might have been drawn as to the value of any particular therapeutic agent.

These figures conform to the general experience that significant paralysis occurs in less than a third of all cases. In the early stages the chances of a diagnostic error are at least as great as the risk of serious paralysis supervening.

The assessment of any therapeutic method depends first on an accurate diagnosis and secondly on the trial of a single agent in a sufficient number of cases and controls to give statistically valid results. It is difficult to carry out a scientific investigation when severe paralysis may ensue if the method on trial proves unsuccessful. In the absence of conclusive proof that a particular agent reduces the risk or severity of paralysis or deformity it is essential to rationalize treatment in accordance with fundamental principles and to avoid

accepting insufficient evidence that some method is of value and consequently to postulate theories in justification.

It is convenient to consider the disease in three stages. First, the inflammatory phase lasting from a few days to a few weeks, when treatment is directed by means of rest and heat to assist Nature to localize and arrest the infection, to relieve pain, and to prevent stiffness or deformity by prophylactic movements. Secondly, the stage of potential recovery of variable duration from a few weeks to as long as two years, when the purpose of treatment is to assist the recovery of the paralysed or weak muscles within the limits determined by the permanent damage in the central nervous system. Thirdly, the stage of chronic disability, when reconstructive operations, appliances, vocational training and the development of compensatory function in surviving muscles are employed to secure resettlement in an occupational and domestic environment suited to the residual capacity of the individual.

Physiotherapy is employed throughout the treatment of this disease, but with a different purpose at each stage. Contrast the use of heat and gentle prophylactic movements in the inflammatory phase with the carefully graduated exercise interspersed with adequate periods of rest during recovery and, again, with the strong and sustained exercise sometimes necessary to obtain adequate compensatory hypertrophy in surviving muscles for ambulation and work in the final stages. The obvious danger is that physiotherapy will be too vigorous and meddlesome in the beginning when hope and enthusiasm run high, and ineffective at the end of a long period of treatment just when it might make all the difference in the final accommodation to a permanent disability.

TREATMENT IN THE INFLAMMATORY PHASE

Poliomyelitis is no exception to the rule that rest from the onset and maintained until the infecting agent has been destroyed gives Nature the best chance to limit the damage. Ritchie Russell, in a preliminary report of his study of the effects of physical activity during the pre-paralytic stage, shows that physical activity of any kind after the onset of infection increases the risk of paralysis and that complete physical rest in bed from the onset of the pre-paralytic stage seems to protect the patient from severe paralysis (Ritchie Russell, 1947). These findings support earlier observations and the generally accepted view that strenuous physical activity coinciding with the onset of the disease increases the severity of the paralysis. But Ritchie Russell finds that the continuation of normal activity such as that of the housewife and clerk after the onset of symptoms increases the risk of severe paralysis to a considerable extent.

It seems reasonable to suppose that if ordinary physical activity is so detrimental early in the disease it may be important to disturb the patient as little as possible until the infection has subsided. I consider that it is of primary importance that we should remember that complete rest is the most effective therapeutic agent to reduce the damage done by the virus. Pain, muscle spasm and paralysis, stiffness and contracture are the result and not the cause of the disease. Treatment involving some disturbance of the patient is necessary to mitigate these secondary effects; but it is essential to do the minimum which will be effective whilst the infection is active.

Rest is attained by complete rest for the body as a whole together with efficient support for the spine and all painful and tender muscles. Of recent years rigid and prolonged splinting has been discarded in favour of minimum immobilization and early movement. As usual the pendulum has swung rather too far. Perhaps we forget that the continuous subconscious contraction of muscles to counter the effect of gravity when the part is inadequately supported does more harm than an occasional purposeful movement. A firm bed, pillows and sandbags are sufficient to rest most of the muscle groups of the trunk and limbs; but there are exceptions such as the biceps brachialis, dorsiflexors of the hand and foot, intrinsic muscles of the hand, &c., which require light plaster or plastic splints to ensure efficient rest.

In the past we emphasized the need to avoid overstretching muscles and to rest them in the relaxed position. It is now generally agreed that the optimum position is midway between contraction and relaxation. This view is borne out by the observations of Young that atrophy of muscles in experimental animals is almost as great when muscles are immobilized in the fully shortened or fully stretched position, or the sensory roots or tendon divided, as when the motor neurones degenerate. This is explained on the basis that if immobilized muscles are maintained in a position of moderate tension proprioceptive impulses stimulate the anterior horn cells and limit the wasting, whereas wasting ensues if the proprioceptive impulses are reduced by overstretching or overshortening the muscles or interrupting the afferent paths (Young, *Lancet*, 1946). We see in this experimental work justification not only for the modern practice of resting muscles in the neutral position; but also for early movements which evoke beneficial proprioceptive impulses. In the early stages, however, it is necessary to strike a balance between the value of rest for the treatment of the infection and of movement to prevent stiffness and undue wasting of muscles.

It is generally agreed that until temperature, pain and muscle tenderness have subsided rest is of primary importance and movement should be limited to what is essential to prevent stiffness. Normally one full-range movement in each direction for all affected joints once or twice a day is all that is required. The signs of active inflammation may clear up in a few days or persist for six weeks and even longer in exceptional cases. The average case takes ten to fourteen days and this is the usual time to start re-educative as distinct from prophylactic movements. The time to commence re-education is a matter of individual judgment.

The afferent impulses which we interpret as pain through connexions in the central nervous system inhibit the anterior horn cells and increase muscle wasting as well as disturbing bodily rest as a whole. Pain counteracts the beneficial effects of general and local rest and must be relieved. Heat and analgesics in the appropriate form and dosage will relieve pain; but it is our experience that the relief is of brief duration unless the painful part is rested efficiently both during exhibition of these therapeutic measures and at all other times. If heat fails to relieve pain the probability is that the method of splinting adopted whether by pillows, sandbags or plaster is inadequate. In our experience moist heat is more effective than infra-red radiation or diathermy. Applications twice or, at most, four times daily are sufficient.

In my opinion the disturbance of the patient associated with two-hourly applications of hot packs together with passive and re-educative movements to prevent so-called alienation, spasm and stiffness of muscles, as advocated by Miss Kenny and others, is liable to retard rather than assist recovery in the early stages and is probably a substantial overdose even for comparatively fit and convalescent patients. I sometimes wonder if the high incidence of muscle spasm in America compared with our experience in this country, where it is comparatively rare, is not explained by too many afferent stimuli reaching a spinal cord in an irritable state consequent upon active or recent inflammation.

We may summarize the treatment of the inflammatory phase as rest for the body as a whole and local rest for the spine and affected muscles in the neutral position; heat in moderation for the relief of pain; and prophylactic movements sufficient to prevent fixed shortening of muscles and œdematous stiffness of joints.

TREATMENT IN THE STAGE OF POTENTIAL RECOVERY

Persistent and patient physiotherapy is the keystone of treatment in this stage and the first six months are all-important. The danger is still of doing too much at the beginning and, if the energy and hopes of both patient and physiotherapist are exhausted in this way, it is probable that too little will be done later on. We might compare the treatment of poliomyelitis with a good runner in the mile race who starts fairly gently and speeds up with each succeeding lap, but holds his greatest effort in reserve for the final sprint. To pursue the analogy further, the after-treatment of a simple fracture is comparable to a short race in which the all-out effort must be built up rapidly for the best results. I think it is important for the patient and physiotherapist to adopt the method of the good mile runner in the treatment of poliomyelitis—more especially perhaps the physiotherapist, who is expected nowadays to use intensive treatment for quick results in some conditions and must adjust herself to both gentle and vigorous work from patient to patient during the day.

After the infection in the spinal cord has been overcome the inflammatory œdema subsides and fairly rapid and widespread improvement occurs in the majority of cases. The recovery in this respect is spontaneous and usually complete at three months; but not much earlier except in mild cases. I do not think anything is to be gained by forcing the pace during this period. Weak muscles should be supported against gravity, especially in the case of the shoulder girdle, arm and hand; and sitting up or ambulation without efficient support should not be permitted if this will throw undue strain on trunk and leg muscles. In my view the important procedure at this stage is frequent and carefully graduated exercises with intervals of effective rest.

At this stage vasomotor changes do not seem to give so much trouble as later on; but it is important to keep the paralysed muscles warm and more especially to avoid exposure and chilling during treatment. Hot packs, warm baths or sinusoidal baths seem to be more useful than radiant heat or diathermy. However, hot packs are time-consuming and at some stages it is not practicable to use baths. In these circumstances a radiant heat cradle or short-wave diathermy should be applied over the trunk or proximal part of the limbs in order to raise the temperature of the body and large blood-vessels. It is our experience that heat applied to a cold paralysed periphery is relatively ineffective and of short duration.

I support Seddon's plea for keeping careful record of the voluntary power of the affected muscles from the beginning of treatment and at regular intervals, as well as for the universal adoption of the classification and system of recording recommended by the Peripheral Nerve Injuries Committee of the Medical Research Council.

Our main concern is with the muscles which have sustained loss of neurones due to permanent damage in the anterior horn cells. It is now generally agreed that overstretching due to lack of support or to splinting in the extended position is harmful; but that full-range movements during the course of treatment are valuable both to prevent fixed shortening of the muscles and to stimulate the stretch reflex.

In the majority of cases electrical stimulation is of little value and may take time which could be employed more profitably in active exercises. Seddon is of the opinion that galvanic stimulation is unjustifiable since if the anterior horn cell is dead the axon will not regenerate, whilst if the anterior horn cell survives the electrical excitability of the muscle is normal and the faradic current, if any, should be used. There is no doubt that occasionally electrical stimulation is useful to start a severely paralysed muscle on the road to improvement. Toomey says that weak muscles in which there is also autonomic vascular disturbance are less excitable than normal and that voluntary contraction cannot be obtained in such muscles unless they are kept in good condition (Toomey, 1947). It is possible that this may explain the benefit which appears to follow electrical stimulation in some cases. Weak muscles respond more readily to the galvanic current because of the predominance of denervated fibres and I think there is a place for it in selected cases.

Whilst we are mainly concerned in this stage with the treatment of flaccid paralysis we meet occasionally cases in which the affected muscle appears capable of quite a strong voluntary contraction; but the patient cannot always initiate such contractions during co-ordinated movement. Lack of co-ordination rather than weakness seems to be the main problem. Although the virus has a selective affinity for the anterior horn cells it may affect any part of the central nervous system, or perhaps it is more true to say that the inflammatory oedema consequent upon the infection may give rise to signs in the adjacent afferent and efferent tracts. In some cases the tendon reflexes are increased and there are other signs of spastic paralysis. In my experience these changes tend to improve and seldom complicate the problem in the late stages.

Toomey suggests that muscle imbalance rather than inco-ordination occurs when one muscle is weaker than its antagonist. He suggests that patients with weak muscles tend to substitute others subconsciously and that further disuse atrophy in the weak muscle occurs. Elkins suggests that muscle dysfunction is due to synchronous contraction of agonist and antagonist due to disturbance of the normal mechanism of reflex innervation and he stresses the importance of the co-ordination of muscle function during treatment (Elkins and Wakim, 1947). There seems no doubt that the problems of the so-called muscle spasm and inco-ordination are related but the precise mechanism has not been fully worked out. The practical implication in treatment is that we should train the co-ordination of muscle groups as well as graduate exercises to strengthen individual weak muscles.

Occasionally oedema of a paralysed limb gives rise to difficulty and should be controlled by elevation, massage and an elastic bandage or stocking. Massage is useful to assist the circulation of paralysed limbs, but it is time-consuming and necessary only in exceptional cases.

TREATMENT IN THE STAGE OF CHRONIC DISABILITY

Some time between six months and two years it becomes obvious that no further improvement is likely to be obtained in the weak muscles by graduated exercise. This is always a difficult decision to take and the point is reached so gradually that it is apt to be overlooked with the result that expectant treatment is continued too long with unnecessary financial hardship to the patient. I think a physiotherapist who has been coaxing weak muscles for many months is liable to underestimate the degree of recovery at this stage and consequently it is important for the medical practitioner to check the voluntary power record frequently at this period. Once the decision has been taken that the limit of improvement has been reached beneficial trick movements should be encouraged and surviving muscles developed by intensive exercises to compensate as far as possible for those which are paralysed or permanently weakened. Reconstructive operations call for physiotherapy during convalescence along the well-established lines which need no special comment, but we must always guard against the over-treatment of these patients in the early stages.

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Dr. P. Bauwens: Being essentially an infectious disease, the diagnosis of A.P.M. in the acute phase is made entirely on clinical and pathological findings.

Electrodiagnostic methods, which amount to a cross-examination of muscles, study only one aspect (the paralytic aspect) of a complex picture. They are, therefore, of no assistance in differential diagnosis, but as the tragic consequences of this disease are related solely to the paralytic phenomena which persist after the others have abated, it is not surprising that these methods play an important part in establishing a prognosis. The electromyographic observations in particular contribute to this.

In the normal muscle fully at rest, no electrical activity is detected either by means of surface electrodes or concentric needle electrodes inserted into the muscle under investigation. During voluntary contraction, action potentials are produced in the muscular component of active motor units. As the contraction increases in strength the electrical disturbances increase both in quantity and in complexity: in quantity because a larger number of motor units enter into play; in complexity because motor units do not fire off simultaneously. Consequently, the electrical by-products to which each motor unit gives rise interfere with those produced by other motor units. The resulting interference pattern is the rule in normal muscles on moderate and maximal effort. Indeed, single discrete motor-unit activity is difficult to produce in the normal muscles.

Taking silence at rest and interfering activity on maximal effort as criteria of normality, it is possible to observe deviations from these criteria and to discuss their prognostic significance. In motor neurone diseases characterized by a progressive destruction of motor units, spontaneous activity frequently occurs in condemned units. Clinically it is seen as fasciculation while in the electromyograph it gives rise to irregular electrical discharges of moderately high amplitude.

The onset of paralysis in A.P.M. is in many ways the history of a motor-neurone disease telescoped into a very short space of time. It is therefore not surprising that spontaneous motor-unit activity of the fasciculation type should occasionally be encountered in the acute phases. In addition to this many muscles appear to be in a state of hyper-irritability. While not actually the seat of spontaneous discharges when the joints which they actuate are placed in comfortable attitudes, these muscles contract on the slightest provocation. Showers of electrical activity accompany these contractions and although I have no evidence to adduce in support of my contention, I suppose that gross exaggeration of this mechanism is the cause of the "spasm" which is described as a prominent feature in some epidemics. Almost any proprioceptive impulse will evoke an electrical discharge in muscles which exhibit this.

With the destruction of anterior horn cells, the number of motor units which operate during muscular contraction decreases. It follows that during activity fewer action potentials are picked up. In bad cases these are reduced to such an extent that there is no longer any sign of interference and the electrical activity manifests itself as a repetition of discrete diphasic potentials on maximal exertion. This activity is clearly due to motor units which are still operative. Their activity may on casual observation appear normal in every respect, yet it may on closer examination exhibit some characteristics of grave prognostic significance. For reasons not yet explained, when the anterior horns are profoundly affected their cells tend to fire off simultaneously, instead of in random fashion. This results in a synchronization of motor-unit activity throughout the muscle. It can be detected by the use of two concentric needle electrodes inserted into a muscle and connected to a double-channel amplifier. Clemmessen and Buchthal who first drew attention to this particular characteristic of paralysis of medullary origin stress its grave prognostic significance in A.P.M.

Although the denervated motor units obviously can no longer respond to volition, they are still capable of some electrical activity. Whereas in the normal motor unit every muscle fibre contracts simultaneously under the influence of impulses reaching them from the nerve fibre, in the denervated unit the muscle fibres behave as autonomous hyperexcitable individuals which appear to react in a repetitive manner to the presence of small amounts of acetylcholine. This fibrillary activity gives rise to characteristic repetitive low voltage spike potentials of short duration. It is diagnostic of axon degeneration.

Those motor units which regenerate after degeneration give rise to highly polyphasic discharges during the stage which precedes recovery. When these occur in paralysed muscles which have previously been silent except for fibrillation they are of good prognosis.

The fact that moderately early recovery can take place in muscles which have at one time shown a marked degree of denervation lends weight to the recent view that this disease may have a more important peripheral neuropathic aspect as distinct from a purely myelopathic aspect than was hitherto suspected. It seems reasonable to suppose that those cases with a purely neuropathic component have a better chance of ultimate restoration than the myelopathic ones. This hypothesis certainly explains why the synchronized motor-unit activity, which points unquestionably to a medullary involvement, is of such very sinister significance.

In several of those cases which have come under my observation of muscles which had recovered power, there co-existed wasting coupled with absent or diminished reflex action and slight incoordination. The puzzling feature was that both maximal exertion and stimulation of the nerve gave rise to normal muscle action potential measurements and no signs of denervation. To explain this, one has to fall back on the assumption that internuncial fibres have been damaged by the disease.

Although not of prognostic or diagnostic importance, it is interesting to note how rapidly fatigue sets in in paretic muscles and how many patients complain of cramp in the lower limbs when these have been affected. The distribution of these painful localized contractions within a muscle tends to indicate a phenomenon of vascular rather than nervous origin.

Miss D. B. Kidd: In the physical treatment of poliomyelitis I have grouped certain important points under the three usually accepted stages of the disease: (a) the early acute stage; (b) the convalescent stage, and (c) the chronic stage.

The early acute stage is essentially the stage of rest. Rest is particularly important where muscle

tenderness, pain and muscle spasm are present, and especially in these cases it appears to be only adequately achieved by firm support, such as is supplied by well-moulded splints of, for example, plaster or perspex.

Muscle tenderness and spasm are also relieved by heat, which at the same time maintains an adequate circulation. My own experience leads me to the conclusion that wet heat is more efficient than dry heat. Short-wave diathermy and radiant heat have proved disappointing and I rely largely on the use of hot wet packs. For these I use towels wrung out in hot water and wrapped round the limb or part. Each towel is left in contact just so long as it takes to prepare the next, and the whole process is continued for approximately ten to fifteen minutes. When towels are in short supply I use three to four layers of lint, or in the children's ward three or four baby's napkins serve the purpose admirably. These hot packs are repeated two or three times daily and precede any other treatment that is being given. They are continued while muscle tenderness persists, usually not longer than three weeks.

At this stage to prevent stiffness and deformity each joint is put passively through its full anatomical range twice daily. Abnormal range, such as is possible in cases of flaccid paralysis, is carefully avoided.

This treatment is begun early, preferably not later than forty-eight hours after the onset of the disease, and is continued until the acute condition subsides. During this stage assisted active movements may gradually be introduced, but detailed progressive re-education is not instituted until the patient has reached the convalescent stage.

The *convalescent stage* is recognized as the stage of re-education, but a correct balance must be maintained between rest and activity and while paralysis or paresis persists, adequate splinting should be retained between treatments.

Before any detailed re-education can be instituted an accurate test of voluntary power should be made and muscles graded according to their power. These tests are repeated at regular intervals. The first test is best carried out over a few days as the acute symptoms subside.

It is not always easy to recognize when a re-education scheme should be introduced. I have found it wiser at first to underrate rather than overrate the power of a muscle. If then fatigue is not observed and progress is satisfactory, exercises can be stepped up as required. Should fatigue occur they should be cut down or stopped at once.

Re-education at first is confined to localized controlled movements only, after which the re-education of co-ordinated movements is introduced. Such a procedure I have found essential in order to obviate the danger of trick movement which only develops the stronger muscles at the expense of the weaker.

The first essential factor in the re-education of these localized controlled movements is the training of the sense of movement in the mind of the patient. This is best taught by carrying out carefully and slowly the desired movement passively while the patient concentrates on what is being done. An adult patient benefits here by being given a little anatomical knowledge. He may then attempt the movement himself, but where his own power is known to be inadequate the movement must be assisted or even wholly achieved by the physiotherapist, otherwise it will either not be achieved at all and the newly learnt sense of movement will be lost, or it will be achieved by the wrong muscles, a trick action resulting. It is also important to ensure that an adequate range of movement is carried out. The whole of the inner range should be used, the muscle being assisted if necessary to work to its innermost point of contraction.

In order to minimize the muscular effort of group action it is necessary to give firm fixation to the fulcrum of movement and to give adequate support to the part moving. As muscle power improves resistance should be added and the number of times the movement is performed increased.

This technique I use regardless of the method employed for re-education, be it under water, in suspension slings or manually, that is, unaided by apparatus. The latter method I always employ at the outset, as a close watch and even closer "feel" is required by the physiotherapist. Of the remaining two methods I infinitely prefer that of suspension slings. In this way the movement is more precise and trick action less likely to develop. Also it is possible to give the patient sufficient rest periods between movements. I have found the pool becomes tiring after twenty to thirty minutes and in this time it is not possible to give adequate re-education where the paralysis is extensive. I therefore prefer to reserve pool therapy for the re-education of co-ordinated movements.

With regard to resisted movements for the development of muscle power, this too is best achieved manually at first as in the early recovery stages the power of the muscle is found to vary from day to day with the mood and condition of the patient. Also a weak muscle will not be able to take the same amount of resistance when contracting through its inner range as when working in its middle range, and such an adjustment can only be made by the physiotherapist's hands. Later, as strength returns, resistance may be made by other means, either simple tension springs or weights. I prefer a simple system of weights and pulleys as these can be more regularly and carefully graduated and an accurate record of progress can be made. Such a record has more than a technical value for it has an encouraging psychological effect on the patient and consequently helps to maintain his co-operation in what must be a long and tedious process.

The re-education of co-ordinated movement is introduced when the patient can achieve the localized movement with the weakened muscle in the gravity-eliminated position. Once introduced they are used in the scheme of treatment alongside of the localized work. These co-ordinated exercises are aimed first at the retraining of group action, the weakened muscle being made to work not only as a prime mover, but also as a synergist and fixator. Following on this, attention is focused on the function of the part, and exercises are introduced involving two or more joints. At the same time occupational therapy comes into the programme, care being taken that trick action is not developed at the expense of the weakened muscles.

Whenever possible the co-ordination exercises are given as free active exercises. Where, however,

muscle power does not allow of this, pool therapy is the best substitute. Should this not be available spring suspension may be used. This has the advantage over ordinary sling suspension in that movement may now be carried out in any plane.

It should be recognized that where suspension sling or spring therapy is employed any simple apparatus may be used, such as the single or double balkan beam. These can easily be fixed up over the patient's bed in the ward, and in suitable cases arrangements can be made for the patient to carry out periods of exercise on his own during the day. But unsupervised treatment is undesirable in the early stages.

Before leaving the treatment of the convalescent stage I should like to speak for a moment on the importance of retraining the postural sense in the upright position. This is necessary in a great number of patients, but it is to the cases of spinal and abdominal involvement that I wish to draw attention. I have found that patients benefit, even in the most severe cases, by attempting to maintain the sitting posture for a few moments at a time at an early date. I therefore introduce the taking of this position over the side of the bed after two to three months; at first it is only included in the treatment two or three times a week. Adequate support is always given, in some instances the patient being literally held up.

The chronic stage is reached when the patient has ceased to make progress over a period of two to three months, and this may be eighteen months to two years or more from the onset of the disease. It is the stage of residual disability, and fortunately many patients never come to this, making a perfect or almost perfect recovery, and requiring only to be hardened off by class work and occupational therapy before return to a normal life.

The chronic stage concerns those who are to be crippled in some degree for life. When this stage is reached it is essential that patients old enough to understand have their condition clearly explained to them. The right moment must be carefully selected to avoid psychological disturbance and is the responsibility of the medical practitioner. Following on this I have found it essential to make drastic changes in treatment. All localized controlled work is stopped and emphasis is laid not only on the co-ordination work previously instituted, but also on the development of trick action which hitherto has been forbidden. In this way the patient is able to make progress in function and is stimulated to further effort.

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The President (Dr. W. S. Tegner) said that he thought Dr. Cooksey's advocacy of moist heat in treatment seemed to give them a rational clue to any value there might be in the Kenny treatment.

Dr. Tegner asked Dr. Bauwens whether in his opinion anterior poliomyelitis was a reversible process and could recovery take place if once an anterior horn cell was knocked out. This was an important point to consider when the value of electrical stimulation in treatment was discussed.

Dr. P. Bauwens replied that, while damage to an anterior horn cell might be permanent, he believed that there was evidence in this disease of lower motor neurone damage without anterior horn cell involvement, and for this type of damage he used the term infantile paralysis.

Dr. J. Barnes Burt: Perhaps one of the chief advances in the treatment of poliomyelitis in the last few years has been the use of the hot pool. In the U.S.A. where this treatment was first in general use, it is considered that hospitalization is shortened by one or two months. The hot pool provides two essential elements for improving the condition of the limbs: (a) Relaxation of muscles; (b) even support of the weakened limbs. Another important factor is the excellent psychological effect. The joy of the children when placed in the hot pool has to be seen to be believed! This factor is, to a certain extent, missed in the Hubbard tank, although the tank has some advantages. It is far cheaper to run, and is not so tiring for the nurses. Special skill has to be exercised by the hydrological nurses. It is quite a different process to assisting passive movement, carried out on a couch, and special training is required. Where one limb is very weak, or has been encased in plaster, Lowman's boards are useful. The temperature of the water ought to be about 98° F., although 102° F. is the optimum for the relaxation of muscles. At a higher temperature than 99° F. the nurses in the pool find it very exhausting, and at this temperature there is less liability for the patient to suffer from thermal debility. If possible all hot pools ought to be provided with a gantry and sling. To carry a paralysed adult, or heavy child, down wet steps, is a great tax on the strength of the nurses, and is apt to frighten the patients.

In the hot pool at Bath, during the last few months of 1947, forty to fifty treatments per week were given to patients in the convalescent stage of poliomyelitis.

Dr. Basil Kiernander said that it was his personal experience that a number of cases of poliomyelitis in which the faradic response of muscles had disappeared had shown, in due course, a return of this faradic response. In these cases, to his mind, it was definitely worth while stimulating the paralysed muscles with interrupted galvanism to keep the muscle fibres well developed in possible regeneration.

He had used short-wave diathermy to the affected muscles for the relief of pain in it and in a number of these cases it appeared to cause considerable relief, but the relief in this way was no higher than for those in which hot packs were employed.

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Muscle tenderness and spasm are also relieved by heat, which at the same time maintains an adequate circulation. My own experience leads me to the conclusion that wet heat is more efficient than dry heat. Short-wave diathermy and radiant heat have proved disappointing and I rely largely on the use of hot wet packs. For these I use towels wrung out in hot water and wrapped round the limb or part. Each towel is left in contact just so long as it takes to prepare the next, and the whole process is continued for approximately ten to fifteen minutes. When towels are in short supply I use three to four layers of lint, or in the children's ward three or four baby's nappies serve the purpose admirably. These hot packs are repeated two or three times daily and precede any other treatment that is being given. They are continued while muscle tenderness persists, usually not longer than three weeks.

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Dr. J. Barnes Burt: Perhaps one of the chief advances in the treatment of poliomyelitis in the last few years has been the use of the hot pool. In the U.S.A. where this treatment was first in general use, it is considered that hospitalization is shortened by one or two months. The hot pool provides two essential elements for improving the condition of the limbs: (a) Relaxation of muscles; (b) even support of the weakened limbs. Another important factor is the excellent psychological effect. The joy of the children when placed in the hot pool has to be seen to be believed! This factor is, to a certain extent, missed in the Hubbard tank, although the tank has some advantages. It is far cheaper to run, and is not so tiring for the nurses. Special skill has to be exercised by the hydrological nurses. It is quite a different process to assisting passive movement, carried out on a couch, and special training is required. Where one limb is very weak, or has been encased in plaster, Lowman's boards are useful. The temperature of the water ought to be about 98° F., although 102° F. is the optimum for the relaxation of muscles. At a higher temperature than 99° F. the nurses in the pool find it very exhausting, and at this temperature there is less liability for the patient to suffer from thermal debility. If possible all hot pools ought to be provided with a gantry and sling. To carry a paralysed adult, or heavy child, down wet steps, is a great tax on the strength of the nurses, and is apt to frighten the patients.

In the hot pool at Bath, during the last few months of 1947, forty to fifty treatments per week were given to patients in the convalescent stage of poliomyelitis.

Dr. Basil Kiernander said that it was his personal experience that a number of cases of poliomyelitis in which the faradic response of muscles had disappeared had shown, in due course, a return of this faradic response. In these cases, to his mind, it was definitely worth while stimulating the paralysed muscles with interrupted galvanism to keep the muscle fibres well developed in preparation for possible regeneration.

He had used short-wave diathermy to the affected muscles for the relief of pain in the acute phase and in a number of these cases it appeared to cause considerable relief, but the percentage of cases relieved in this way was no higher than for those in which hot packs were employed.

muscle power does not allow of this, pool therapy is the best substitute. Should this not be available spring suspension may be used. This has the advantage over ordinary sling suspension in that movement may now be carried out in any plane.

It should be recognized that where suspension sling or spring therapy is employed any simple apparatus may be used, such as the single or double balkan beam. These can easily be fixed up over the patient's bed in the ward, and in suitable cases arrangements can be made for the patient to carry out periods of exercise on his own during the day. But unsupervised treatment is undesirable in the early stages.

Before leaving the treatment of the convalescent stage I should like to speak for a moment on the importance of retraining the postural sense in the upright position. This is necessary in a great number of patients, but it is to the cases of spinal and abdominal involvement that I wish to draw attention. I have found that patients benefit, even in the most severe cases, by attempting to maintain the sitting posture for a few moments at a time at an early date. I therefore introduce the taking of this position over the side of the bed after two to three months; at first it is only included in the treatment two or three times a week. Adequate support is always given, in some instances the patient being literally held up.

The chronic stage is reached when the patient has ceased to make progress over a period of two to three months, and this may be eighteen months to two years or more from the onset of the disease. It is the stage of residual disability, and fortunately many patients never come to this, making a perfect or almost perfect recovery, and requiring only to be hardened off by class work and occupational therapy before return to a normal life.

The chronic stage concerns those who are to be crippled in some degree for life. When this stage is reached it is essential that patients old enough to understand have their condition clearly explained to them. The right moment must be carefully selected to avoid psychological disturbance and is the responsibility of the medical practitioner. Following on this I have found it essential to make drastic changes in treatment. All localized controlled work is stopped and emphasis is laid not only on the co-ordination work previously instituted, but also on the development of trick action which hitherto has been forbidden. In this way the patient is able to make progress in function and is stimulated to further effort.

To re-educate walking we must frequently use ambulatory splints. There are very few cases who cannot attempt walking. I find it preferable not to introduce it while the patient is still making satisfactory progress in recumbency. When it is eventually introduced it is quite remarkable to note in many cases a distinct improvement in some muscles which had seemingly already reached their maximum power.

The President (Dr. W. S. Tegner) said that he thought Dr. Cooksey's advocacy of moist heat in treatment seemed to give them a rational clue to any value there might be in the Kenny treatment.

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[April 14, 1948]

Infantile Cerebral Palsy

By PHILIP RAINSFORD EVANS, M.D., M.Sc., F.R.C.P.

INCIDENCE

THE incidence of infantile cerebral palsy has been estimated by Duryea (1941) to be 50 patients per 100,000 of the population in the United States of America. According to Phelps (1941) the figures are similar in urban and rural districts, and may be expressed as: 7 born each year per 100,000 population:—1 dies in infancy; 2 are mentally defective; 4 are educable, of whom 1 is mildly, 2 moderately, and 1 severely afflicted.

Thus for every 100,000 people there are probably about 30 children who are moderately affected and who need special education and therapy. At this rate London would have to cope with over 2,000 children with cerebral palsy who need these special methods, and perhaps another 3,000 who are so severely handicapped mentally or physically that they need to be cared for in institutions. It must, however, be emphasized that we have no figures upon which an estimate of the incidence in this country can be based. A survey is needed. All one can say at present is that the two residential units open in England accommodate some 50 children, and that the pathetic quest of the parents for adequate treatment for their handicapped sons and daughters is marked by recurring disappointment.







Classification.—Cerebral palsy is a condition arising in early life, due to imperfect development or damage of the central nervous system above the segmental level, and characterized by motor disability. This disability may be associated with spasticity, rigidity, or flaccidity of the muscles, with ataxia, or with involuntary movements.

W. J. Little (1843*b*) gave an excellent description of cerebral palsy in one of his "Lectures on Deformities of the Human Frame" in 1843. In a Paper read to the Obstetrical Society in 1862, he elaborated his early observations (1843*a*) on the association of prematurity and asphyxia with this type of disease. He has received and deserves great credit for his accurate and original observations but it is unfortunate that recognition of his merit has taken the form of a chapter heading: "Little's Disease (Spastic Diplegia)." He did not describe a uniform and clear-cut disease, but an association between certain abnormalities of labour and the newborn period and diverse mental and physical abnormalities seen later in life. Some of the children exhibited spastic diplegia, others paraplegia, hemiplegia, triplegia, fits, mental defect, and involuntary movements. The term athetosis was not invented until 1874.

The classification of these conditions has become so much confused that it is possible for diplegia and paraplegia to be used in the same sense in the same table (Brockway, 1936), while a simple division of cases into spastic and athetoid has been known to arouse in a neurologist the unbecoming passion of anger.

Classification may first be considered topographically. In Table I, diplegia has currently two different meanings, and here we will use the term paraplegia and quadriplegia instead. I will not attempt to defend the logic of this conventional division of paralyses. Starting with monoplegia, a one-stroke, we go on to a half-stroke which is twice as extensive as a monoplegia; a diplegia or two-stroke is actually four times as extensive as a one-stroke but affects twice as many limbs as a half-stroke.

TABLE I.—NOMENCLATURE ACCORDING TO LIMB-INVOLVEMENT

Limbs involved	Neurological Term	American Therapists' Term
 OR 	Monoplegia	Monoplegia
	Hemiplegia	Hemiplegia
	Triplegia	Triplegia
	Paraplegia	Diplegia
	Diplegia	Quadriplegia*

*The term "quadriplegia" is customary, although "tetraplegia" is more in keeping with Greek prefixes of the other types.

We are in more difficulty when we come to disturbance of function (Table II).

TABLE II.—CLASSIFICATION BY DISTURBANCE OF FUNCTION
Neurological Phelps (1938, 1941) and others

Spastic	Spastic
Flaccid or atonic	Flaccid
Rigid (lead pipe)	Rigid (plastic)
Double athetosis	Athetoid { Non-tension Tension
Double hemiplegia }	
Ataxia	Tremor
Chorea	Ataxia
	Chorea

The chief difficulty is to reconcile the neurologists who consider double hemiplegia an important group, and double athetosis to be rare, with those who follow Phelps in classifying 40% of cerebral palsies as athetoid and in paying little attention to double hemiplegia.

The features which distinguish double hemiplegia from spastic quadriplegia are shown in Table III.

TABLE III
Spastic quadriplegia Double hemiplegia

Paralysis symmetrical	Paralysis asymmetrical
Legs worse than arms	Arms worse than legs
Intelligence often slight	Intelligence often normal

Neurologists agree that athetoid movements often appear late in the course of a hemiplegia, particularly in the upper limb. Ford (1946) points out that an extensive lesion of a cerebral hemisphere produced experimentally during the growth period produces defective development of the lenticular nucleus. Phelps, on the other hand, asserts that muscular tension is induced, voluntarily and involuntarily, to suppress athetoid movements. Involuntary movements are unpleasant, we have all seen the "good hand" holding the other and preventing it moving, in unilateral athetosis and occasionally in Sydenham's chorea. I think that if one saw only children under the age of 3 years one would often diagnose double hemiplegia. In older children athetosis is the striking thing, although it may be masked by muscular tension. "Athetoid" is a useful descriptive term directly related to treatment, but the pathology underlying it awaits elucidation.

It might be thought that the behaviour of the plantar reflex would be decisive in indicating which cases were hemiplegia with associated athetosis, and which were primarily athetoid. But the vagaries of this reflex during recovery from acute hemiplegia in childhood indicate that it is not a good differential sign. The reflex in athetoid children is difficult to test satisfactorily, and may be extensor or flexor. Its behaviour, in fact, is like that in the newborn infant, before the extensor reflex has become firmly, although temporarily, established.

Spastic muscles superficially resemble those exhibiting athetoid tension, but a distinction can usually be made on examination. Spastic tension can be overcome only by putting the muscle in a position in which it is not stretched, or by force. Athetoid tension relaxes under verbal persuasion, and gives way to gentleness instead of force. When the child is asleep the muscles are relaxed, and the athetoid limb may be moved in any direction. Even during sleep the spastic muscle tightens when it is stretched. In rare cases of severe athetosis, really amounting to dystonia, muscles may remain tense during sleep.

I have mentioned that the signs in double hemiplegia are not symmetrical. Symmetry need not here be introduced into the description as a separate feature but it is relevant to considerations of aetiology (McGovern and Yannet, 1947).

An indication of the relative incidence of the various types may be obtained by analysis of 115 cases seen by me recently (Table IV). Many presented because of need for special education or treatment, so that the milder types, e.g. the slight hemiplegia or paraplegia which does not prevent a child from going to an ordinary school, are inadequately represented. There are probably some errors in the table as not all patients are easy to classify. I once diagnosed athetosis in a child of 1 year and 4 months. I saw him again one and a half years later and it seemed more likely that he was a hyperactive mental defective, and not an example of cerebral palsy at all.

TABLE IV.—CLASSIFICATION OF 115 CASES OF INFANTILE CEREBRAL PALSY

Type	Number	%
Monoplegia	3	3
Hemiplegia	10	9
Spastic para- or quadri-plegia	43	37
Flaccid quadriplegia	3	3
Athetoid	45	39
Chorea	1	1
Ataxia	4	3
Mixed types	6	5

Most cases fall into the spastic and the athetoid groups, and I propose not to discuss the less common ones further.

ÆTIOLOGY

Except in such studies as Collier's (1899) classical paper on cerebral diplegia, now half a century old, careful pathological investigations correlated with clinical analysis are lacking. I hope Stewart will extend his laborious work, the substance of which was related in his Presidential Address to the Neurological Section in 1942, in this direction.

Purely clinical studies, of which Little's was the first, are more numerous but less convincing. Collier (1924) pointed out that although some factors commonly recur in the case-histories (one may take prematurity as an example) they are not constant and are not, in other children, followed by nervous complications.

Taking the 115 cases (see Table IV) we may note: 8 (7%) had suffered from erythroblastosis foetalis. The neurological sequelæ of nuclear jaundice have been studied by Fitzgerald *et al.* (1939) and by Stiller (1947). In my experience the paralysis in these cases is likely to be severe, and quadriplegic. Chorea or athetosis may develop. Rhesus incompatibility did not appear to be a causative factor in the other cases. Dr. I. A. B. Cathie investigated the mothers of 38 of them without finding evidence of such incompatibility. 4 (3%) were subjects of arrested hydrocephalus, which usually produces spasticity. 3 (3%) had encephalitis, which tends especially to produce hemiplegia or choreo-athetosis. 2 (2%) suffered from hæmorrhagic disease of the newborn, and may have had cerebral hæmorrhages.

Thus the cause of the condition was apparent in 15% of the whole. Considering only the spastic and athetoid groups (79 cases) in the remaining 85%:

There was no familial history and no unusual number of consanguineous marriages in this series. There is a hereditary influence (Bell and Carmichael, 1939; Haldane, 1941) but it is not numerically important.

Prematurity (judged by birth-weight) occurred in 49% of spastics, 32% of athetoids and 8% of a control group of children not suffering from organic nervous disease. Further study of this relationship is necessary.

The incidence of asphyxia and complicated labour was high in the athetoid group.

Table V shows the proportion of affected children who were firstborn, the anæsthetic and forceps rates, and the incidence of neonatal asphyxia of sufficient severity for the parents to remember particulars of it.

TABLE V

	Athetoid	Spastic	Control
Firstborn	73%	33%	24%
Anæsthetic	85%	45%	38%
Forceps	38%	16%	10%
Neonatal asphyxia ..	97%	21%	0%

These results will be reported in greater detail elsewhere, but it is difficult to avoid the conclusion that cerebral anoxia is closely connected with the occurrence of athetosis, while one must accept Freud's (1897) and Collier's (1899, 1924) view that an early defect of neuronal development is probably the cause of spastic paraplegia and quadriplegia.

CLINICAL PICTURE

Characteristically the condition is not diagnosed until the age of 9 months or 1 year. This is partly because the first thing the parents notice to be wrong with the child is that he does not sit up at the right age, and perhaps partly because we use for the examination of these infants a technique which has been designed to show up abnormalities of the adult nervous system.

There may be an early history of a spastic limb or an abnormal posture, of icterus gravis, of atelectasis or cerebral hæmorrhage, of convulsions in the first two weeks of life, but the story is often merely one of delay in the acquisition of motor and postural skills. The child does not sit at the usual age of 6 or 8 months, at 10 months he is seen by a doctor who can find nothing much wrong with him and counsels patience. The first birthday brings comments from the relatives and causes reflection. The infant is taken again to the doctor who advises a consultation or a visit to hospital where the diagnosis is made. Adductor spasm will have developed at this time, and will be apparent when the child is lifted up, but in athetoid cases the characteristic serpentine movements may not be clearly distinguishable from infantile and physiological inco-ordination until the age of two years.

Table VI shows the delay in sitting, walking, feeding, talking and acquiring control of the excretions in the first six years. These figures are taken from examination of the records of 59 children who were being considered for admission to a special school and who were preselected as being the more promising cases of those who were too severely affected to go to an ordinary school.

TABLE VI.—AGE WHEN CHILD LEARNED TO SIT AND WALK WITHOUT SUPPORT, TO USE A SPOON, TO TALK (USING SIMPLE SENTENCES), AND BECOME CONTINENT OF URINE AND FÆCES DAY AND NIGHT

Year of life	1st	2nd	3rd	4th	5th	6th	7th or later	Data incomplete
Sat	7	23	5	11	2	2	6	3
Walked	0	2	6	8	5	6	20	12
Used spoon	0	11	14	10	3	2	9	10
Talked	0	7	13	7	7	4	4	17
No incontinence ..	1	18	8	5	3	3	2	19

Bold figures are definitely abnormal

The state of the muscles and reflexes may be compared with the normal and with the familiar example of anterior poliomyelitis (Table VII).

TABLE VII

Condition	System involved	Voluntary contraction of agonist	Tone, on attempted movement		Effect of concentration	Tendon jerks	Plantar reflexes
			Agonist	Antagonist	Other muscles		
Normal	None ..	N	+	—	Synergy	Good	N
Polio.	L.M.N. ..	0	0	0	0	0	0
Spastic	Pyramidal ..	N	+	+	+ or 0	Good	+
Athetoid	Basal ganglia	0 or ±	±	±	±	Bad	±

N = normal; 0 = nil; + = increase; — = diminution; ± = variable

This is perhaps over-schematic but it may be found a useful summary.

Associated features.—Associated neurological defects are supposed to be common, but I do not find many, except those connected with the organs of special sensation. One does, however, encounter:

Squints: These are very common, and are often variable and may be alternating. The “wandering eye” may stop its peregrinations when general physical treatment has achieved some success, but orthoptic treatment may be needed. Blindness may occur, with or without optic atrophy.

Deafness, particularly to certain tones, is common. Its importance has been emphasized by Phelps (1941).

Speech defects are extremely common. They may be due to: (a) Mental defect; (b) deafness; (c) interference by the disease with normal right- or left-handedness; (d) spasticity of the tongue and other muscles of speech; (e) athetosis of tongue, palate, larynx and particularly respiratory muscles. Anyone who has been in an iron lung will realize how much slow, regular, involuntary respiratory movements interfere with speech; it is much more difficult for the severe athetoid who has to contend with irregular involuntary movements. Speech therapy obviously needs intelligent diagnosis in these cases, as well as great skill and patience.

Epilepsy is fairly common.

Dysphagia and dribbling are troublesome in severe cases.

Hydrocephalus has been mentioned. Microcephaly also may accompany spastic palsies, and with true microcephaly there is of course severe mental defect.

General health.—Little remarked that the sufferer from this condition was often said to be the healthiest in the family. He also noticed that “the frame is often lean and wiry, but not wasted”, which is certainly true of athetoids. Spastic children are often thin and may be wasted, but they do not engage in the activities of the athetoids and may be very fat. Treatment of the obesity may be necessary before they can be taught to walk. Dental caries is often gross and usually untreated.

As might be expected, athetoids need more food than spastics. The latter, with their slow and difficult movements, may suffer from the cold. During the fuel crisis last year, a special school was imperfectly heated, and 10 of the 11 boarders had chilblains, while none of the 8 day-attenders suffered in this way.

Urinary incontinence needs special attention. The main thing is to note the individual patient’s habits and means of expressing the desire to micturate. The mother usually works this out herself. The child should feel secure and comfortable on the toilet seat, so that he may relax and empty the bladder completely. Otherwise he will only pass a small quantity in the lavatory but will flood the bed when he is put back in it. This is not, of course, naughtiness or a desire to attract attention, but is caused by relaxation in comfort with a full bladder.

Psychology.—The psychological aspects of the problem are as important as the physical. One must recognize, and avert or treat apathy, aggressiveness, and lack of confidence. Morale may be boosted by apparently small things, like the provision of a school cap, such

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one where the child is brought daily by his mother. The former is probably best for the very young, and for those where the home environment is bad, or the parents unintelligent. The day institution is good in that the child leads a normal home life, and the mother gets thorough instruction in the management of her child. In fact, in this type of centre the mother rather than the child, is taught, and this is very important, because, in order to prevent relapses, treatment programmes must continue for years. These day centres are doing very well in Australia. Whatever the type of centre, it must provide full facilities for mental education as well as physical rehabilitation, and it should bear as little resemblance to a hospital as possible, one of the key-notes being that the child must not be looked upon as sick in the ordinarily accepted sense of that word.

As has been said, treatment must continue for years in most cases, and so a great deal devolves upon parents. All that centres can do is to correct the worst of the defects, to provide the correct management programme, to give the right appliances, and to instruct the parents how to carry on, the child being brought back every six months or so for review and change of programme where necessary.

Before proceeding to a more detailed treatment of any specific type of cerebral palsy there are some general points which are applicable to all.

The earlier treatment can commence the better, and an age of 1 year is certainly not too young. There are obvious risks of maldagnosis in starting at this age, and it is not easy to determine whether the child be intelligent or not, but there is one very great advantage in that the child does not develop bad movement patterns in the endeavour to overcome his handicap himself, and further the right environment can be ensured. In the older child these bad habits of movement superimposed upon the original handicap are very difficult to deal with and make the best results almost impossible of attainment.

These children must be enabled to sit up in a chair as soon as possible. Many, if not all of them, cannot sit unsupported at the age they would normally be able to do so, and they are too often allowed to lie on their backs all day staring at the ceiling or the sky. They thus are unable to gain normal childish experience by observing their surroundings. Such a chair is specially made so that the child can sit well into it and be completely supported as to the back and head, and he may be strapped in if necessary.

Where there is not gross athetoid movement, the child should be encouraged to roll and kick on the floor, and he may be allowed to crawl, but he should not be allowed to stand or walk until his reablement programme is well advanced.

Respiration is often irregular or of a faulty pattern, and steps must be taken as early as possible to correct this since without correct movements of breathing a child will have difficulty in swallowing and in speaking.

Proper feeding is often overlooked. In addition to poor respiration the movements of tongue and palate are often restricted or irregular. Swallowing is therefore difficult and slow and these children often do not get sufficient to eat. Thus, great patience must be shown, and the child should be given plenty of time to deal with small mouthfuls. Again, it is often not realized that some of these children have impaired palatal sensation, and the spoon is often placed too far into their mouths, with the result that they choke and may refuse their food.

As treatment programmes are long and may continue for months at a time, it is most important that the child's interest in his treatment should be aroused and maintained. To this end his rehabilitation must be made as attractive as possible, and one good plan is to teach him his exercises, &c., to the sound of an easily learnt tune preferably sung to him in order that he may get the sense of the words as well.

Due to the natural enthusiasm of teachers and therapists there is a danger of overworking the child and overtaxing his powers of concentration. Programmes must therefore be carefully worked out with this in mind, and adequate rest periods provided.

Passing to the spastic type of cerebral palsy, it will be found that these children are often extremely fearful. They must therefore, at all times, feel perfectly secure. Treatment tables must be wide enough to give them this feeling of security, and they must be handled firmly and competently. In contradistinction to the athetoid child they often need a considerable amount of urging. They should be carefully examined in an effort to discover exactly which muscles and muscle groups are involved in the disease, which are hypotonic and which have become weakened due to their being stretched by the affected antagonist. They should not be allowed to stand or walk until their abdominal and back muscles have been given sufficient strength by exercise to give them proper pelvic control, since it may be found that tight hamstrings and adductors may be due to weak abdominals allowing the pelvis an exaggerated tilt. At the same time a scheme of exercises is made out for the re-education of their limb muscles, and when as much improvement in pelvic control as possible has been obtained they can pass to practise in sitting unsupported, kneeling, standing, and finally walking. It is always useful to get as much aid from gravity as possible by posturing the child in his

as other boys have, to the patients in a hospital school. I must mention the danger of overstimulating athetoid children, stressed by Carlson (1937). They cannot stand a lot of treatment in a day, the journey to the hospital may by itself make them so tense and inco-ordinate that treatment is impossible. It is well to remember that they are at their worst when they are taken to see the doctor.

On intelligence testing, I can do no more than repeat the warning that ordinary testing is unfair to these children with motor, sensory, and speech defects, and that it may be impossible to assess the intelligence without some weeks of observation. The response to treatment is thus more useful than a single psychometric session. E. S. Evans (1946) found over 60% of spastics and under 10% of athetoids ineducable.

Selection of cases.—In selecting cases the following general points should be taken as favourable: Age 1 to 12 years, but especially 1 to 5 years; normal or high intelligence; perseverance and ability to concentrate, which may compensate for an inferior intelligence; sociability; no epilepsy; no sign of progressive nervous deterioration.

If facilities for treatment are limited, it is better to concentrate on the mildly and moderately affected, for the severe cases take an immense amount of the time of therapists, teachers, nurses and porters.

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Some Points in Management of Infantile Cerebral Palsy

By JOHN H. CROSLAND, M.R.C.S., L.R.C.P.

THE management of a case of cerebral palsy differs in many respects from that of infantile paralysis or from that where the defect is purely sensory, e.g. blindness or deafness. In poliomyelitis there is a motor disability which can arise at almost any age, but there are no sensory defects, and there is usually no brain damage. In blindness and deafness there is usually one specific sensory disability, all other aspects of the case being relatively normal. In cerebral palsy, however, there is a motor disability of greatly varying severity, there may be sensory loss, such as partial or total deafness, and sight may be adversely affected. In addition, there may be such damage to the brain as to produce a subnormal intelligence, and one may be confronted with a psychological problem to make things even more difficult.

Thus, at the outset, one must try to get a picture of the total disability of any particular child, and try to assess the effect of one defect on the other. One must also get an idea of the child's background and his home conditions so that a composite picture forms in the mind. In the first instance the child is examined physically and placed in one or other of the five types of cerebral palsy according to Phelps. This may not always be possible at the first examination, though usually it can be done. Next, he must be seen by a child psychologist, and an estimation made of his intelligence. Here it must be said that only a psychologist used to making proper allowance for the motor disability and the usual lack of normal childish experience will be able to give a correct assessment of the I.Q. Defects of sight and hearing should be attended to by the appropriate specialist, and external aids provided where necessary.

It is not yet clear which type of treatment centre is the better, the purely residential or the

Section of Urology

President—WALTER W. GALBRAITH, M.B., F.R.F.P.S.

[January 22, 1948]

DISCUSSION ON ADVANCES IN THE TREATMENT OF URÆMIA

Mr. Ronald Reid

ABSTRACT.—Uræmia is common, little is known of its actual nature and treatment has therefore been unsatisfactory. The kidney is not only an organ of excretion but guards the chemical and physical constitution of the extracellular fluids.

In uræmia, urea and other products of metabolism including the toxic phenols accumulate. That the physical and chemical composition of the extracellular fluids, excluding protein, can be influenced by contact across a semi-permeable membrane is the basic concept of the treatment of uræmia by dialysis, whether by means of the artificial kidney or by peritoneal lavage.

The principles of treatment of uræmia are: (1) To remove the cause. (2) Reduce the load on the kidney. (3) Assist or take over the function of the failing kidney in the hope that it may recover. (4) To relieve symptoms without thereby prejudicing recovery.

Dialysis can be effected by peritoneal lavage or by conducting the circulating blood through a tube of semi-permeable membrane. The composition of the dialysing fluid is of the utmost importance the aim being to keep the physical and chemical balance of the extracellular fluid within the normal range and to encourage the diffusion of toxic metabolic products. The excessive use of parenteral fluids and diuretics in uræmia may be harmful. A number of cases of peritoneal dialysis are described.

RÉSUMÉ.—L'urémie est fréquente, et sa vraie nature est peu connue, par conséquent, son traitement est resté peu satisfaisant. Le rein est non seulement un organe excrétoire, mais protège aussi la constitution chimique et physique des liquides extra-cellulaires.

Dans l'urémie l'urée et d'autres produits du métabolisme, y compris les phénols toxiques, s'accumulent. Le principe fondamental du traitement de l'urémie par la dialyse, soit par un rein artificiel ou par le lavage péritonéal, est la possibilité d'influencer la constitution physique et chimique des liquides extra-cellulaires par le contact à travers une membrane semi-perméable.

Les principes du traitement de l'urémie sont 1° l'élimination de la cause, 2° la diminution de la charge sur le rein, 3° aider ou remplacer la fonction du rein défaillant, dans l'espoir qu'il guérisse, 4° le soulagement des symptômes sans empêcher la guérison.

La dialyse peut être effectuée par le lavage péritonéal ou par le passage du sang circulant par un tube de membrane semi-perméable. La composition du liquide dialysant est de la plus haute importance. Le but est de maintenir l'équilibre chimique et physique du liquide dans les limites normales, et de favoriser la diffusion des produits toxiques du métabolisme.

L'emploi exagéré de liquides parentéraux et de diurétiques dans les urémies peut être nuisible.

L'auteur décrit plusieurs cas de dialyse péritonéale.

Прогресс в лечении уремии

Доктор Р. Рид.

КОНСПЕКТ.—Уремия хотя и частое явление, но о ее существенном свойстве мало известно и оттого лечение не удовлетворительное. Почка не только орган для выделения, но она также охраняет химический и физический состав экстрацеллюлярных жидкостей.

При уремии накапливаются мочевины и другие продукты метаболизма, включая токсические фенолы. Лечение уремии диализом, будь то при помощи искусственной почки или же перитонеальным промыванием, основывается на том, что контакт через полу-проницаемую перепонку влияет на физический и химический состав экстрацеллюлярных жидкостей, за исключением белков.

Принципы лечения уремии: 1/ устранить причину; 2/ уменьшить нагрузку почки; 3/ помочь или перенять функцию слабеющей почки в надежде на излечение, и 4/ облегчить симптомы, не мешая излечению.

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exercises. Thus he may be placed head downwards on a tilted table where the pectoral muscles are spastic. Again, where the dorsiflexors of the foot are weak, as they often are, he may be placed on his abdomen with his legs at right angles to the table.

In the child with athetosis the key-note of management is relaxation. If he can be taught to relax efficiently, he can lose a great deal of his unwanted movements. It is very important that these children should have really adequate rest periods because of the greatly increased amount of energy consumed by this uncontrolled movement. When relaxation has been achieved as well as may be, he must be taught new movements of the affected limbs which are purposive movements under his own volitional control.

Relaxation must first be taught in the prone position. At first a child may find it easier to relax on one or other side, but eventually he must be taught in all lying positions. When this has been acquired, he must be taught to relax in the sitting position, using a properly constructed chair. After this, sitting balance and then standing balance must be taught, and not until these have been achieved should he be allowed to walk.

Many cases of athetosis develop a "tension" which is thought to be a voluntary effort to control the unwanted movements. In these cases the teaching of relaxation will at first increase the unwanted movement, but a great deal of this should be lost if the child follows the regime outlined. It should be said, however, that, particularly in older children, this tension may be extremely difficult to overcome, and it may be necessary to proceed with training in spite of it.

Occupational therapy is an important part of the management of most types of cerebral palsy. It has, of course, little part where the arms are unaffected. Its main sphere is to teach the child to carry over into every day actions what has been taught him by the physiotherapist. That is to say, he is taught to feed himself, and to dress himself, and this is carried out by practice with various feeding aids, such as drinking straws, special plates, spoons, &c. In learning to dress, the child will first practise buttoning, lacing, &c., on models held immovably in frames. He is also taught the movements of writing, and, if it is thought he will not be able to achieve this legibly, he is taught to use a typewriter. While the athetoid child is being taught these skills the occupational therapist must see that the rest of his body is maintained in the relaxed position.

As most of these children have a speech defect they will need the services of a speech therapist. One of the most important parts of this person's job, apart from speech training, is to ensure that the child's facial expression is as normal as possible, in order to increase the child's subsequent social chances and his value in the labour market.

Appliances of various kinds are used. Space forbids any detailed description, but a word should be said concerning leg braces. These are used to a very great extent in the pioneer schools in America. Their use must be regarded as corrective rather than as mere props, and it should always be remembered that it is a great psychological boost to get a child on his feet as soon as possible.

At present no unduly optimistic views as to the results of treatment should be entertained. Practically all children who are educable benefit from treatment, but the amount of such benefit varies enormously. The lowest aim is to make the child self-sufficient as far as dressing, feeding, and amusing himself is concerned. Even this will take an intolerable burden from parents. A small percentage will benefit to the extent of being able to take their places in normal life from the intellectual point of view. A somewhat larger percentage can be trained to craft standard, and thus be enabled to earn their own living, but it must be emphasized that both these latter percentages add up to a small proportion of the whole.

The President (Dr. W. S. Tegner) said that the subject was most important, and one was forcibly reminded that many of these children have been regarded as mentally deficient and condemned to a life in institutions when subsequent experience has shown that they are often educable.

Dr. J. Euan Dawson asked what could be done for the spastic child who suffered from bad athetoid movements, for he had known several cases where the anguish suffered from the perpetual movement was such as to undermine the child's general health, and no conservative treatment had in these cases been of any avail.

Dr. J. Shulman stated that the optimum age to begin treatment appeared to be the age-group 1 to 4 years, but in view of the wide interest now being taken in this problem, many applications for treatment were made on behalf of patients of much older age-groups. Was there any age at which one could definitely say it is useless to begin treatment?

Dr. Crosland, in reply to Dr. Dawson, stated that each case must be taught individually how to relax.

In reply to Dr. Shulman he said that there was a sharp fall in the progress charts if treatment was delayed to the later age-groups.

В нашей машине это более усовершенствовано и установлен тщательный контроль над втечением и вытечением крови, которые совершенно синхронизированы. Для улучшения анализа насос, контролирующий течение крови, присоединен к барабану таким образом, что 10 миллилитров крови входит и выходит из машины на каждое полное вращение барабана. Производимое таким образом движение дает удовлетворительный анализ, но машина слишком громоздкая и несмотря на точный контроль кровяного течения, целлофановая трубка может растянуться и допустить накопление крови.

Оттого мы изобрели вторую, более компактную, машину, в которой целлофановая трубка проходит через серию пластинок, а анализирующая жидкость выпускается через серию отверстий в центре пластинок. Таким образом, анализирующая поверхность того же размера может быть смата в машину 18 дюймов длины и 9 дюймов вышины и вместе с тем объем крови в машине не может быть увеличен.

Конечный успех анализа будет зависеть от состава анализирующей жидкости. Опыт показал, что жидкости одинакового электролитического состава, хотя и изотоничны, не остаются изоосмотическими. Это зависит от того, что глюкоза, которая употребляется для поддержания осмотического давления, быстро всасывается в больного. Это производит перегружение кровообращения больного и ввиду этого вода в анализирующей жидкости не может быть задержана. Потому очень важно найти нетоксичное, не-анализирующее вещество, которое было бы способно поддерживать изо-осмотическое давление.

EXTRACTO.—En el método de Kolff de diálisis sanguínea se usa un tambor giratorio para extender una fina película de sangre sobre la extensa superficie de un tubo de celofana, que actúa de membrana dializadora.

En nuestro aparato esto ha sido ventajosamente desarrollado, pero además, un control exacto permite que el aflujo y salida de sangre sean exactamente sincronizados. Para mejorar la diálisis, las bombas que regulan la corriente sanguínea están conectadas con el tambor, de modo que 10 c.c. de sangre entran y salen de la máquina en el transcurso de una rotación completa del tambor. La agitación así producida mejora considerablemente la diálisis, pero el aparato en conjunto es voluminoso y a pesar del cuidadoso control de la corriente sanguínea, el tubo de celofana puede distenderse permitiendo cierta acumulación de sangre.

Para evitar este inconveniente, hemos construido una segunda máquina, mucho más compacta, en la cual el tubo de celofana atraviesa una serie de placas que presentan unos orificios en el centro, a través de los cuales es inyectado el líquido dializable. De este modo, la misma extensión de superficie dializante es comprimida en una máquina de 45 centímetros de longitud por 22 centímetros de altura, con la particularidad de que el volumen de sangre dentro de ella no puede ser aumentado.

El éxito final de las diálisis dependerá de la composición del líquido dializable. La experiencia ha demostrado que los de un mismo carácter electrolítico, aunque isotónicos, no permanecen iso-osmóticos. Esto es debido a que la glucosa usada para mantener la presión osmótica, se difunde rápidamente al interior del paciente, con lo que el líquido dializable es incapaz de retener el agua, resultando de ello una sobrecarga de la circulación del paciente. Es por tanto esencial la búsqueda de una sustancia no tóxica e indializable, que sea capaz de mantener una presión iso-osmótica.

Dr. E. G. L. Bywaters and Dr. A. M. Joekes

ABSTRACT.—Two recently evolved methods of dealing with uræmia (a) by dialysis through cellophane (the Kolff artificial kidney), and (b) through the peritoneal membrane, were described.

Dr. E. G. L. Bywaters and Dr. Joekes described the results obtained over a period of fifteen months using the Kolff artificial kidney. It consisted of a cellophane tube rotating in a Ringer bath, through which blood flowed from an artery and back to a vein. The bath water (100 l.) contained glucose 1.5-2.0 grammes % and chloride, sodium, bicarbonate and potassium in physiological concentrations. The most suitable type of case was one of tubular or "lower nephron" disease (e.g. pigment nephrosis), since complete recovery was possible. 12 cases had been dialysed, including 2 complete recoveries, detailed in full. The maximum amount removed was 92 grammes urea in seven and a half hours, at a blood flow through the cellophane tube of about 60 ml./min. This reduced the blood urea to about half its previous level. Factors working against recovery included pre-existing pneumonia, widespread oedema and sepsis; one subdural hæmorrhage occurred, but no other bleeding complications due to heparin were seen. 0.5-1.0 grammes heparin was used per patient. The pump was used to fill a gravity-feed burette for returning blood to the patient, and in the later patients right auricular pressure obtained by cardiac catheterization was used to control flow. Amidopyrine, penicillin, nembutal and calcium gluconate were also given. A high-caloric non-protein diet was prescribed afterwards in an effort to obviate nitrogen accumulation due to endogenous protein catabolism.

RÉSUMÉ.—Description de deux méthodes de traitement de l'urémie récemment développées:

(a) La dialyse à travers le cellophane (rein artificiel de Kolff).

(b) La dialyse à travers la membrane péritonéale.

Les Drs. E. G. L. Bywaters et Joekes rapportent les résultats obtenus pendant 15 mois par l'emploi

Диализ можно совершить или же перитональным промыванием, или же пропускаем обращаемой крови через трубку с полу-проницаемой перепонкой. Состав диализирующей жидкости весьма важен, так как нужно удерживать физическое и химическое равновесие экстрацеллюлярной жидкости в пределах нормы и поощрять диффузию токсических продуктов метаболизма. Чрезмерное употребление подкожных инъекций и мочегонных средств может быть вредным.

Описаны несколько случаев перитонального диализа.

EXTRACTO.—A pesar de ser la uremia un síndrome común, su naturaleza es muy poco conocida y su tratamiento, por consiguiente, insatisfactorio. El riñón no es solamente un órgano de excreción: mantiene además la composición físico-química de los fluidos extracelulares.

En la uremia, hay un acúmulo de urea y otros productos del metabolismo, inclusión hecha de fenoles tóxicos. El hecho de que, exceptuando las proteínas, la composición físico-química de los líquidos extracelulares pueda ser influenciada por contacto a través de una membrana semipermeable, constituye la base del tratamiento de la uremia por diálisis, ya sea mediante el riñón artificial o por lavado peritoneal.

Los principios para el tratamiento de la uremia son: (1) Eliminar la causa; (2) Disminuir la sobrecarga renal; (3) Asistir o hacerse cargo de la función del riñón claudicante con la esperanza de que pueda todavía recuperarse; (4) Tratar los síntomas sin que con ello se comprometa la recuperación.

La diálisis puede efectuarse por lavado peritoneal o bien conduciendo la sangre circulante a través de un tubo de membrana semipermeable. La composición de los fluidos dializables es de la más alta importancia, ya que la finalidad es el conservar el equilibrio físico-químico de los líquidos extracelulares dentro de los límites normales y favorecer al propio tiempo la difusión de los productos tóxicos del metabolismo. El uso excesivo de fluidos parenterales y diuréticos en la uremia puede ser peligroso. Se describen además una serie de casos de diálisis peritoneal.

Dr. E. M. Darmady

ABSTRACT.—Kolff's method of dialysing blood makes use of a rotating drum to spread a thin film of blood over large dialysing surface (a cellophane tube).

In our machine, this has been further developed, but a strict control is kept on the inflow and outflow of blood, which are exactly synchronized. To improve dialysis, the pumps controlling the flow of blood are geared to the drum so that 10 ml. of blood enters and leaves the machine for every complete rotation of the drum. The agitation thus produced results in successful dialysis, but the machine is bulky and, in spite of this careful control of blood flow, the cellophane tube may expand and allow accumulation of blood.

We have, therefore, developed a second and more compact machine, in which the cellophane tube is run through a series of plates, the dialysing fluid being injected by a series of ports in the centre of the plates. In this way, the same sized dialysing surface can be compressed into a machine 18 inches long and 9 inches high, and at the same time the volume of blood in the machine cannot be increased.

The ultimate success of dialysis will depend on the composition of the dialysing fluid. Experience has shown that those of a similar electrolytic pattern, although isotonic, do not remain iso-osmotic. This is because the glucose used to maintain the osmotic pressure diffuses rapidly into the patient. This results in overloading the patient's circulation, because water can no longer be held in the dialysing fluid. A search for non-toxic, non-dialysing material capable of maintaining an iso-osmotic pressure is therefore essential.

RÉSUMÉ.—La méthode de Kolff pour la dialyse du sang consiste en l'emploi d'un cylindre tournant pour étendre une couche mince de sang sur une grande surface dialysante (tube de cellophane).

Dans notre machine cette idée a été développée plus loin, mais l'arrivée et le débit sont strictement réglés et synchronisés exactement. Pour améliorer la dialyse les pompes réglant la circulation sont engrenées avec le cylindre de telle façon que 10 ml. de sang entrent et sortent de la machine à chaque tour complet du cylindre. L'agitation ainsi produite donne une dialyse satisfaisante, mais la machine est volumineuse, et malgré le réglage soigneux de la circulation, le tube de cellophane peut se dilater et permettre au sang de s'accumuler.

Nous avons donc inventé une seconde machine, plus compacte, dans laquelle le tube de cellophane passe entre une série de plaques, le liquide dialysant étant injecté par une série d'orifices au centre des plaques. De cette façon une surface de la même grandeur peut être incluse dans une machine longue de 18 pouces (45 cm.) et haute de 9 pouces (22 cm.), et d'autre part, il est impossible d'augmenter le volume de sang dans l'appareil.

En fin de compte, le succès de la dialyse dépend de la composition du liquide dialysant. L'expérience a montré que des liquides de composition électrolytique semblable, même s'ils sont isotoniques, ne restent pas iso-osmotiques, parce que le glucose employé pour maintenir la pression osmotique se diffuse rapidement dans le malade. Ceci surcharge la circulation du malade, parce que le liquide dialysant ne peut plus tenir l'eau. Il est donc essentiel de chercher une substance non toxique et non dialysable capable de maintenir une pression iso-osmotique.

Доктор Дармади.

КОНСПЕКТ.—При Методе Кольфа для диализирования крови применяется вращающийся барабан для распространения токой фильмы крови на большой диализирующей поверхности /целлофановая трубка/.

Transperitoneal Dialysis

By RONALD W. REID, F.R.C.S.

URÆMIA is a symptom which is easily recognized and is a common cause of death, and yet little is known of the actual nature of the condition. It follows that treatment, not being based on sound knowledge, has been unsatisfactory. There is little doubt that many factors are involved including: (1) The accumulation of toxic products of metabolism. (2) Alterations in the osmotic pressure of the body fluids. (3) Dehydration or its opposite. (4) Alterations in the balance of electrolytes. (5) Changes in the acid-base balance.

Professor Gamble of Harvard, to whom all interested in this subject owe a debt for his magnificent work on the extracellular fluids, states that the kidney is very inadequately described as an organ of excretion. He states: "Were removal of waste products its only function a much simpler mechanism would suffice. Its complexity of design and intricacy of function are required for the construction and accurate defence of extracellular fluid, on the chemical consistency of which depends the successful operation of intracellular processes."

I like to look upon the kidney as a guardian of the environment of the body cells, as responsive and delicate as the most sensitive thermostat in the maintenance of a constant temperature, but infinitely more comprehensive in its action.

The composition of the body fluids is shown in Gamble's famous diagram (fig. 1). The body fluids amounting to about three-quarters of the body-weight can be looked upon as

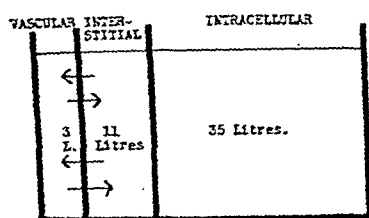


FIG. 1.—Body fluids compartments (after Gamble).

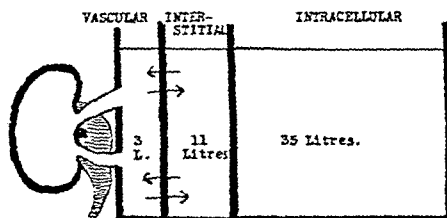


FIG. 2.—Diagram of kidney in action.

existing in three compartments, although interchange is constantly going on: (1) The intracellular fluid, 35 litres in an 11-stone man. (2) The interstitial fluid, 11 litres. (3) The intravascular fluid, 3 litres.

Potassium and phosphorus are the ions concerned in the composition of the intracellular fluid, and it seems certain that the cell membrane in contrast to the capillary is impervious to most electrolytes.

The relationship of the kidney to the fluid in the vascular system which is in the closest and most sympathetic contact with the rest of the extracellular fluid in the interstitial compartment is shown in fig. 2.

The functions of the kidney are to maintain the physical and chemical constancy of the body fluids and to eliminate waste products of metabolism. As its function fails from disease, lack of water or salt or some other essential factor to its proper action, so the composition of the body fluids changes and waste products accumulate. The exact nature of the changes is in some doubt but it is known that a number of products of metabolism appear in increased quantities in the blood stream, including urea and phenols. Urea is not toxic to man in the concentration found in the blood in many cases of profound uræmia, but generally speaking, the amount of urea in the blood is a rough index to the severity of the uræmic state. Harrison and Mason have shown that free phenols accumulate in the body fluids in uræmia and that their concentration rises as toxæmia progresses.

Although the nature of the metabolic toxins remains obscure there is reason to believe that they are dialysable, that is to say, pass freely across a semi-permeable membrane such as the capillary wall or the peritoneum. I have confirmed the observation made years ago that the urea content of the blood and of natural ascitic fluid are almost identical.

That the physical and chemical composition of the extracellular fluids, excluding protein, can be influenced by contact across a semipermeable membrane is the basic concept of the treatment of uræmia by dialysis, whether by means of the artificial kidney or by peritoneal lavage.

du rein artificiel de Kolff. Il consiste en un tube de cellophane tournant dans un bain de solution de Ringer, ou circule du sang venant d'une artère et rentrant dans une veine. Le liquide dans le bain (100 litres) contient de 1.5 à 2.0 grammes pour cent de glucose et des concentrations physiologiques de chlorure, de sodium, de bicarbonate et de potassium.

Les cas qui bénéficient le plus de ce traitement sont ceux de maladie tubulaire ou du "néphron inférieur" (les néphroses pigmentaires par exemple), car la guérison complète est possible. Douze cas ont été traités par la dialyse, avec deux guérisons complètes. Ces cas sont rapportés en détail. La plus grande quantité d'urée éliminée fut 92 grammes en sept heures et demie, le courant de sang passant par le tube étant d'à peu près 60 ml. par minute. De cette façon l'urée sanguine fut réduite à environ la moitié de son taux original. Les facteurs opérant contre la guérison étaient, entre autres, des pneumonies existant d'avance, des œdèmes extensifs et la sepsie. Une hémorragie sous-durale fut observée, mais aucune autre complication hémorragique due à l'héparine, dont 0.5 à 1.0 gramme fut employé pour chaque malade. Une pompe fut employée pour remplir une burette à gravitation pour rendre le sang au malade, et chez les derniers cas la pression auriculaire droite fut contrôlée par la cathétérisation du cœur pour permettre d'ajuster la circulation. L'amidopyrine, la pénicilline, le nembutal et le gluconate de calcium furent employés comme médicaments additionnels. Un régime riche en calories et sans protéine fut prescrit après le traitement, pour éviter l'accumulation de protéine due au catabolisme de la protéine endogène.

доктор Байвотерс и Доктор Джекс.

КОНСПЕКТ.—Описаны два недавно испытанных способа для лечения уремии: 1/ путем диализа через целлофан /искусственная почка Кольфа/ и 2/ через перитонеальную оболочку.

Доктор Байвотерс и доктор Джекс описывают результаты полученные в применении искусственной почки Кольфа в течение 15 месяцев. Для опыта употреблялась целлофанная трубка, вращающаяся в ванне Рингера, через которую протекала кровь из артерии и обратно в вену. 100 литров воды в ванне содержало 1.5 - 2.0% глюкозы и хлористый натрий, сода и калий в физиологических концентрациях. Наиболее подходящий случай оказалась болезнь трубок или нижнего нефрона, т.е. пигментозный нефроз/ ввиду того, что в этом случае полное выздоровление было возможно. Было продиализировано 12 случаев, причем два из них дали полное выздоровление. Автор дает полные детали. Максимальное количество удаленной мочевины было 92 грамма в 7½ часов, причем количество протекаемой крови через целлофанную трубку было приблизительно 60 миллилитров в минуту. Это уменьшило количество мочевины в крови приблизительно на половину предыдущего уровня. Факторы предупреждающие выздоровление включали: заранее существующую пневмонию, обширные отеки и сепсис. В одном случае появилось субдуральное кровоотечение, но в общем гепарин не вызывал никаких других кровоотечений. Для возвращения крови больному автор пользовался насосом, который нагонял бюретку путем тяжести. У некоторых больных для контроля течения употреблялось правое предсердечное давление путем сердечной катетеризации. Амидопирин, пенициллин, нембутал и глюкозный кальций тоже были применены.

После опыта была прописана диета, содержащая большое количество калорий с полным отсутствием белков с намерением предупредить накопление азота вследствие эндогенного белкового катаболизма.

EXTRACTO.—Se describen dos métodos recientemente desarrollados para tratar la uremia: (a) por diálisis a través de un tubo de celofana (el riñón artificial de Kolff) y (b) por diálisis a través de la membrana peritoneal.

Los doctores E. G. L. Bywaters y Joeques reseñan los resultados obtenidos con el empleo del riñón artificial de Kolff durante un período de quince meses. El aparato de Kolff consiste en un tubo de celofana giratorio a través del cual la sangre procedente de una arteria circula en dirección a una vena. Este tubo gira sumergido en un baño de solución de Ringer (100 litros), conteniendo de 1.5 a 2 gramos por % de glucosa y cloruros sódico y potásico y bicarbonato, en concentraciones fisiológicas. El caso más adecuado fue uno de lesión tubular (nefrosis pigmentaria), con el que fue posible obtener la curación completa. Doce casos dializados, incluyendo dos curaciones completas, son minuciosamente detallados. La cantidad máxima de urea separada fue 92 gramos en 7½ horas, con una corriente sanguínea de 0.060 litros por minuto pasando a través del tubo. Con esto se logró reducir a la mitad la cantidad de urea en sangre. Entre los factores que pudieron comprometer el completo restablecimiento, mencionan un caso de neumonía preexistente, otro con extenso edema y otro con sepsis; se presentó una hemorragia subdural pero no se vio ninguna otra complicación hemorrágica a consecuencia del empleo de la heparina, que en dosis de 0.5 a 1 gramo fue administrada a cada paciente. La sangre era devuelta al paciente desde una bureta que se llenaba por medio de una bomba y en los últimos casos el flujo sanguíneo se reguló de acuerdo con la presión auricular obtenida por cateterización cardíaca. Fueron administradas amidopirina, penicilina, nembutal y gluconato cálcico. Una dieta no proteica, rica en calorías, fue prescrita a continuación, al objeto de evitar la acumulación de nitrógeno debida al catabolismo de las proteínas endógenas.

William Abbott of Detroit and his collaborators have studied peritoneal dialysis in the last few years and have shown that urea nitrogen diffuses quite rapidly into fluid which has been injected into the peritoneum, and that nephrectomized animals can be kept alive in a relatively normal state for over a week by intermittent peritoneal lavage.

Fine, Frank and Seligman of Boston have studied peritoneal perfusion for the treatment of uræmia during the last few years, and have shown that continuous peritoneal irrigation with the proper fluid is a satisfactory method of treating uræmia, and they point out that the control of electrolyte and fluid balance is at least as important as the elimination of toxins.

In peritoneal dialysis I have, as far as possible, used the method when I felt there was some hope of recovery. I have only used intermittent peritoneal lavage which I have held to be more satisfactory for reasons which I will discuss later.

CASE I.—Our first case was that of a woman aged 37 who had anuria following an incompatible blood transfusion. She was treated by vast quantities of fluid intravenously and admitted to our hospital with anuria of nine days' duration. She was œdematous and drowsy, with a blood urea of 253 mg.%. The kidneys were washed out by cystoscopy. A high spinal anæsthetic was given to no avail, and as the patient's condition was rapidly deteriorating and renal tenderness was very marked on both sides, it was decided to decapsulate the kidneys, and this was done on the tenth day. Œdema of the skin, muscle and perinephric tissues was pronounced. Both kidneys were so firm that on decapsulation the renal substances burst. After the operation a rubber catheter was inserted into the peritoneal cavity and 2,000 c.c. of twice normal saline dripped in slowly. Only 1,100 c.c. were recovered and by this time the patient had begun to pass urine, and there was also an escape of urine from the renal wounds. The next day 1,000 c.c. of double strength saline was run into the peritoneal cavity and only 205 recovered, and the process was further repeated. In all 6,000 c.c. of twice normal saline were put into the peritoneal cavity slowly and allowed to escape, and 2,500 c.c. were recovered containing just over 6 grammes of urea in all, but a great deal of fluid escaped into the dressings. The woman began to pass urine freely after decapsulation and there is no doubt that peritoneal dialysis had little to do with her recovery, but we were satisfied with our experience because first, the woman recovered, and secondly, we had shown that urea could be recovered by peritoneal dialysis. The patient has been followed up since and is normal in all respects.

CASE II.—The second suitable case did not appear for six months. In September 1946 a man, aged 57, was admitted to hospital semi-comatose. Twenty years previously he had undergone a right nephrectomy and about ten days before admission he was seized with nausea and vomiting and gradually his urine output had declined. For twelve hours before admission he had passed no urine whatever. He had a tender, palpable and slightly enlarged left kidney and a blood urea of 268 mg.%. It was thought he had an obstruction of the pelvo-ureteric junction and catheter drainage up the ureter was unsatisfactory. The patient went downhill rapidly, was completely comatose and vomiting copiously. A rapid nephrostomy was performed through the cortex of the greatly distended kidney. A rubber catheter was introduced into the peritoneal cavity and twice normal saline was run in slowly for twelve hours and then allowed to escape naturally. Peritoneal dialysis was continued in all for seventy-two hours, a total of 6,350 c.c. double-strength saline being run into the peritoneal cavity, but only 1,600 c.c. were recovered containing 6·7 grammes of urea. In the meantime the decompressed kidney began to function freely and in twenty-four hours produced 10 litres of urine. The blood urea fell from 268 to 57 mg.%, and a week later the kidney was explored at leisure and obstruction due to aberrant vessels relieved.

In this case again peritoneal dialysis had little to do with the patient's recovery. We lost very little fluid by leakage, and as we put over 6,000 c.c. into the peritoneal cavity and recovered only 1,600 a great deal of the saline was absorbed and excreted by the kidney.

An interesting feature is that the concentration of urea in the peritoneal efflux was higher than that of the blood (fig. 5), and another interesting point is that the chloride concentration of the dialysing fluid which was 0·18 grammes to begin with, rose to 0·26 grammes at the end of dialysis. It seems that there was a selective absorption of water which accounted for the high level of urea and chlorides in the peritoneal washings.

CASE III.—The third case was a man of 62 who had a carcinoma of the prostate for which a resection was done in March 1945, followed by treatment with stilbæstrol. In October 1946 the patient was admitted with the pelvic floor infiltrated with growth. He was uræmic with a blood urea of 262 mg.%. It was considered that the lower ends of the ureters were blocked by growth. Forced fluids were employed without improvement and it was decided that the man might be tided over the crisis by peritoneal dialysis.

We considered that in the last cases there was evidence that too much chloride had been used in the peritoneal wash, and so in this man normal saline was used. 4,000 c.c. were run into the peritoneal cavity and only 650 c.c. recovered.

2,000 c.c. were used for each dialysis and the efflux contained 450 mg.% of urea in the first specimen and 360 mg.% in the second. It is interesting to note that during this time the blood-urea readings were 203 and 195 mg.% (fig. 6).

Eventually the man died quite suddenly and the post-mortem examination showed massive prostatic carcinoma blocking the ureters and multiple secondaries in the lungs.

CASE IV.—The next case was that of a male aged 58, who was admitted in November 1946 in a semi-comatose condition with an offensive dark brown vomit and diarrhoea, he was in a collapsed condition with a blood-pressure of 70/50. He was treated on general principles for shock and given continuous 5% dextrose saline intravenously and very slowly. He improved slightly and by the

Fig. 3 indicates diagrammatically the contact with the extracellular fluids achieved by means of the artificial kidney.

Fig. 4 shows again diagrammatically the same contact by means of peritoneal lavage. The basic principles which I consider are involved in the treatment of uræmia: (1) To remove the cause where possible. (2) To reduce the load on the kidney. (3) To assist or take over the function of the failing or failed kidney in the hope that it may recover. (4) To relieve symptoms without thereby prejudicing recovery.

(1) *Removal of the cause.*—In so many cases the cause is unknown, but a careful survey of the patient in general and of his urinary tract in particular should be made, keeping in mind infections and obstructions.

(2) *The load of the kidney may be eased* by reducing protein breakdown, thus diminishing the metabolic products to be excreted. Protein intake may be limited and at the same time sufficient carbohydrates should be given to prevent the body having to break down proteins

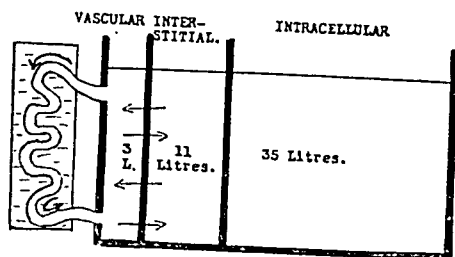


FIG. 3.—Diagram of artificial kidney in action.

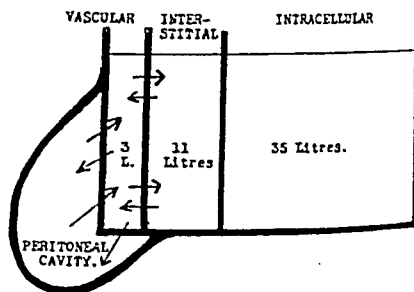


FIG. 4.—Diagram of peritoneal dialysis.

to provide energy for ordinary needs. In starvation protein is rapidly broken down after the carbohydrate supply is exhausted. Therefore, starvation especially of carbohydrates is detrimental to uræmia and a low-protein and high-carbohydrate diet should be advised. Neither should the circulation be overloaded with fluids or diuretics. Water and urea, the best diuretics, usually exist in plenty unless the patient has suffered loss from diarrhoea, vomiting and sweating.

It must not be forgotten that the relief of symptoms is one of the supreme duties of the doctor, but I would utter a warning against, first, the use of more than the minimal quantities of sedatives, and secondly, against the forced ingestion of fluids particularly by the intravenous route, especially in the presence of cardiac failure.

(3) To turn now to the assistance of the failing or failed kidney, it must first of all be assured that the organ receives sufficient quantities of oxygen, and for this reason any serious degree of anæmia should be corrected by blood transfusion. Cardiac failure must also be corrected, if possible, because the kidney cannot do its work without sufficient blood-pressure. Many patients suffering from uræmia, especially the aged, are deficient in hæmoglobin.

There are two methods of making intimate contact with the body fluids across semi-permeable membranes, for the purpose of removing diffusible toxins and restoring the physical and chemical constitution of the extracellular fluid. First, by peritoneal lavage, and secondly, by conduction of the blood through a semi-permeable tube immersed in a suitable solution. I will briefly go over the history of these methods.

In 1914, Abel, Rowntree and Turner performed artificial kidney experiments on dogs using a tube of semi-permeable membrane immersed in physiological saline solution. Gantner in 1923 used peritoneal lavage for the treatment of uræmia in dogs after bilateral ligation of ureters, following the demonstration by Putnam that urea, creatine and other crystalloids diffused into peritoneal fluid from the blood. So far as I know the story of the artificial kidney and of peritoneal dialysis starts with the workers I have mentioned.

The most impressive contribution came from Bliss, Kasteler and Nadler in 1932, who found that dogs after bilateral nephrectomy survived on an average three days unless peritoneal lavage was used. Peritoneal lavage extended life to between thirteen and sixteen days, and in one instance over 9 grammes of urea were removed from the blood stream in twenty-four hours. These workers used saline and found, and I think this point is of very great importance, that the animals died of generalized œdema, especially severe in the lungs.

In 1938 Wear, Sisk and Trinkle, used peritoneal perfusion for the treatment of two cases of uræmia following carcinoma of the bladder. They reduced the blood urea but vast quantities of perfusing fluid were used to recover rather small amounts of urea.

In recent years the work originated by Abel, Rowntree and Turner has been revised, extended and developed by Kolff of Kampen.

skin and lungs 1½ litres. It appears that by sweating, respiration and dialysis the body was deprived of about 3 litres of fluid and this no doubt accounted for the disappearance of œdema. The amount of urea recovered in all was 38.5 grammes.

In this case a considerable quantity of urea was removed from the blood stream by dialysis; more interesting still is the examination of the reaction of the blood chlorides to the dialysis with glucose in water. Much chloride was removed.

Fig. 9 shows the changes. It is estimated that 52 grammes of chloride were extracted from the body, again we had failed to take proper care of the electrolyte and water balance in the extracellular fluid.

Another point of great interest arises from the examination of the samples of fluid taken every quarter of an hour. It appears that equilibrium is reached in about two hours.

It was resolved that should another case turn up further care must be taken with the composition of the dialysing fluid, so that on the one hand water and salt were not lost to the body, nor were water and salt excessively added.

CASE VI.—In February 1947, a male patient, aged 51, was admitted to hospital with anuria of thirty-six hours' duration. A week before admission his doctor thought he was developing pneumonia and gave him a supply of sulphadiazine. He took 24 grammes in six days and had been instructed to drink plenty of fluid, but had not done so. On examination he appeared fairly fit for his age, he had a slightly furred tongue and was tender on palpation in both loins. His chest was clear. A catheter was passed but no urine obtained.

Large quantities of alkaline fluids were given by mouth and the next day no urine had been secreted and a cystoscopy was performed. There was considerable œdema of both ureteric orifices, some fine brownish crystals were seen in the bladder and on the left side crystals and clot were protruding from the orifice. These crystals were subsequently identified as those of sulphadiazine.

During the day the blood urea rose from 99 to 117 mg. % and his clinical condition deteriorated throughout the day and he began to show signs of marked œdema of the lungs. At 6 p.m. a cystoscopy was performed but catheters would not pass up the ureters and so it was decided to do a nephrostomy on one side. The kidney was exposed and a clear rush of urine followed the incision of the pelvis and a Cabot's nephrostomy was performed. After the operation a plastic tube with side holes was introduced into the recto-vesical pouch and the bronchial tree sucked out by bronchoscopy. On return to the ward 2,000 c.c. of 5% glucose in normal saline was run rapidly into the peritoneal cavity. Here we were using saline to avoid chloride depletion and glucose to maintain osmotic pressure.

Half-hourly samples of fluid were taken for analysis and the remaining fluid sucked out three hours later. Fig. 10 shows the urea changes. 1,650 c.c. were recovered. The dialysis was repeated with the same solution, but as the patient complained of pain the tube had to be withdrawn and a fine

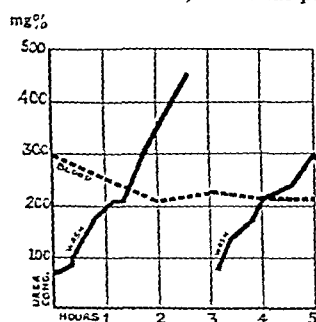


FIG. 8.—Case V.

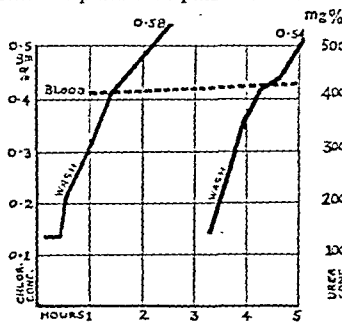


FIG. 9.—Case V.

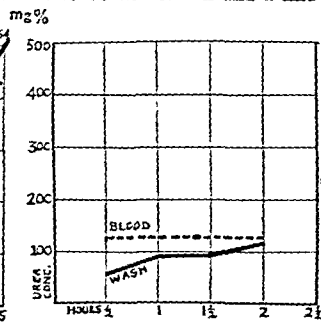


FIG. 10.—Case VI.

trocac passed into the peritoneal cavity in the right iliac fossa, and 1,600 c.c. of fluid drained by this route. Suction of the bronchial tree had to be performed again while the patient was in bed as his chest was very bubbly.

By the next morning the blood urea was 117 mg. % and his general condition much improved. 277 c.c. had drained from the nephrostomy and in the evening he passed 700 c.c. of clear urine. Thereafter the patient improved rapidly and was discharged from hospital well.

A biopsy of the kidney taken at operation showed sulphadiazine crystals in the tubules.

In this patient the bronchopneumonia or œdema of the lungs from which he was suffering was the most dangerous condition, and I think the repeated suction of the bronchial tree was the main factor in his recovery. The dialysis, while it was beneficial, cannot be regarded as having been a success. While it was functioning the blood-urea level was reduced but it rose again after the dialysis was discontinued. Only 4 grammes of urea were recovered from the efflux.

This is just a brief account of my experience with peritoneal dialysis, and the results are not impressive. My accounts are not complete and I have given but a few of the hundreds of estimations which were done in the laboratory while the cases were treated. I should like to pay tribute to the work done by Mr. Roland Jones and Dr. J. Penfold who helped me. Those undertaking peritoneal dialysis must be prepared to stay up all night.

What have we gained from our experience?

next day it was found his blood urea was 460 mg.% and he had only passed a few c.c. of urine. The next day the patient's condition began to deteriorate again and although the cause of his uræmia was not known it was decided that pending further investigation to reach an accurate diagnosis, peritoneal dialysis was justified to assist the failing kidney.

A rubber tube was passed down through the abdominal wall into the lower part of the peritoneal cavity and 2 litres of double strength saline were run in as quickly as possible and left in the pelvic cavity for six hours. The running in of the fluid at this rate did not cause discomfort. The fluid was gently sucked out and the dialysis repeated twice more. 10,000 c.c. of fluid in all were run into the peritoneal cavity and 6,500 recovered and found to contain 18.8 grammes of urea. Fig. 7 shows the blood urea levels and the levels in the washing fluid.

Meantime the patient's condition deteriorated and he became œdematous, especially in the lungs and died two days after admission.

The post-mortem showed gross pulmonary œdema, but a normal liver and apparently normal kidneys. There was no peritonitis. Section of the liver and kidney showed no gross abnormality.

The treatment in this case was unsatisfactory in that no cause was found for the uræmia. It may

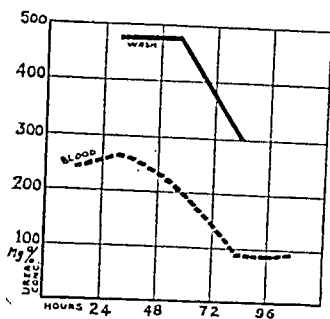


FIG. 5.—Case II.

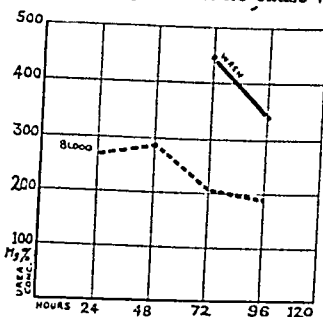


FIG. 6.—Case III.

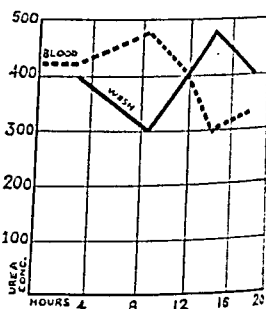


FIG. 7.—Case IV.

have been prerenal in type. We recognized, rather too late, that the man was absorbing huge quantities of saline from the peritoneal cavity, and that like some of the animals used in experimental fields, the cause of death was pulmonary œdema.

It was resolved that should another opportunity for peritoneal dialysis arise, an attempt should be made to avoid overloading the patient with water and chlorides, and we realized also that we had been aiming at the removal of urea and forgetting the necessity of making a real attempt to take care of the physical and chemical composition of the extracellular fluid.

CASE V.—In January 1947 a man, aged 23, was admitted to hospital complaining of diarrhoea, vomiting and malaise. He had a medical history of some length. In May 1943 he was said to have suffered from some form of renal infection and in August 1943 he had been in hospital with œdema of the ankles, feet and face. He was then known to have albumin in the urine and red cells but no casts. Apparently he was diagnosed as a case of nephritis and sent home.

On admission in January 1947 he was pale, ill-looking and drowsy, with a furred tongue and moderate œdema and ascites. His blood-pressure was 180/120 and his urine loaded with albumin. His blood urea was 30 mg.% and hæmoglobin 36%. He continued to vomit and became more drowsy and was given a slow intravenous drip of 5% glucose in saline for three days, and some blood. After this the blood urea fell to 123 mg.%, moist sounds appeared in both lung bases and the infusion was discontinued. The urine output continued to fall and by the evening of the 20th, ten days after admission, his blood urea was 300 mg.%. His condition was rapidly deteriorating and it was decided that the danger period might be tided over by peritoneal dialysis. A plastic tube was inserted into the recto-vesical pouch through a small incision in the right iliac fossa, and on opening the peritoneum urea content of 300 mg.%, identical with that of the blood. Dialysis was started at about 9.30 a.m. with 2,000 c.c. of 5% glucose in water and 1 gramme of novocain run into the peritoneal cavity. It was decided to use glucose and water, a solution with an osmotic pressure sufficient to prevent the loss of large quantities of water into the blood stream, and novocain was added lest the glucose solution caused pain. Samples of this fluid were withdrawn every quarter of an hour for two hours, in order to determine the rate of urea dialysis and the optimum time at which to discontinue and withdraw the fluid. After three hours the dialysis was discontinued and the fluid in the peritoneal cavity sucked out. After a short interval another 2 litres of 5% glucose in water was run rapidly into the peritoneum and retained for a further three hours, samples being drawn off every quarter of an hour.

Fig. 8 shows the blood urea levels and the level in the fluid withdrawn at intervals. The patient's general condition did not improve and he died.

Post-mortem examination showed marked hypertrophy of the left ventricle and slight œdema of both lungs, but not of the subcutaneous tissues. The liver was pale with cloudy swelling, the kidneys very pale with capsules adherent and section showed obvious chronic nephritis.

During the last twenty-four hours of his life the patient passed no urine whatever. 12 litres of 5% glucose in sterile water were run into the peritoneal cavity and in all 13½ litres were recovered. The patient sweated considerably during the day and had hypernæa, so that he probably lost by

also produces agitation. This ensures that a fresh sample of blood is being constantly brought to the dialysing surface. In fact, the success of agitation has enabled me to cut down the size of the drum and the dialysing surface. We have also found that by synchronizing our drums to our pumps so that 10 millilitres of blood enters the machine for each complete rotation, a better and more even film is produced which leads to better dialysis. This machine, however, is bulky and has a large number of points which have to be attended to. The bath water is not only exposed to the air, adding to the chance of becoming infected but also the dialysed products tend to build up in the water and thus slow down dialysis. This has led us to search for a machine of simpler design and we have found that by leading a cellophane tube through a machine in which there is a series of plates 1/16th inch apart a large dialysing surface can be achieved. The flow of dialysing fluid is arranged by means of a number of small tubes in the plates which allow the dialysing fluid to flow from the centre outwards in either direction. Unfortunately this machine does not at the moment produce as satisfactory dialysis as the rotating machine.

The most important of all the factors which control successful dialysis is the composition of the fluid in the dialyser. Hitherto these fluids have been of the simple electrolyte pattern, they have contained salts which are isotonic with normal blood but have added glucose

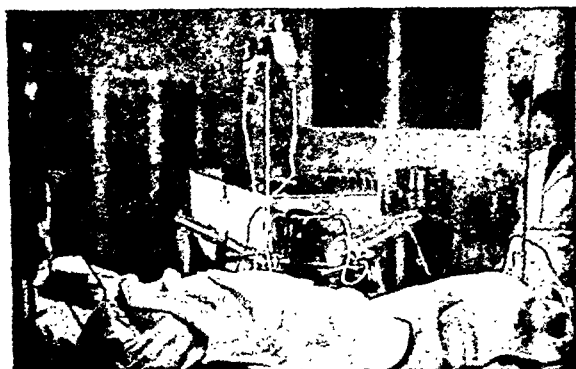


FIG. 1.

FIG. 1.—General view of machine in use. A.—Blood is obtained from radial artery. B.—Blood is restored to a suitable vein.

FIG. 2.—It is essential to control the in and out flow of blood by means of synchronized pumps. The pumps are designed to inject 10 c.c. for every complete rotation of the drum, thus ensuring even distribution of blood over the dialysing surface.

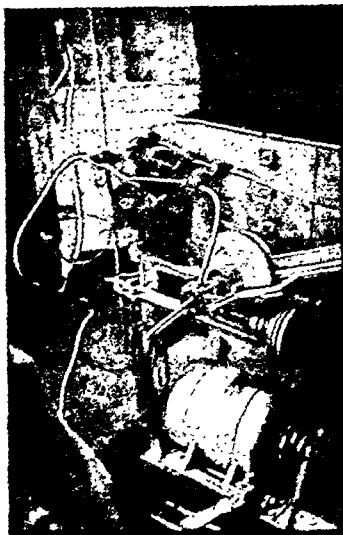


FIG. 2.

to raise the osmotic pressure and although these materials have been used with success in the past, they have one grave disadvantage, that the osmotic action is not maintained, for there is a rapid diffusion of glucose into the patient which is followed by water shift. For example, we have found that whereas we started with 20 litres of fluid in our bath water, this was reduced at the end of two hours' dialysis to 17 litres of which only 1 litre and a third could be accounted for by evaporation. We feel that this flow of water from the bath into the circulation leads to circulatory discrepancies and possibly cardiac failure. We therefore feel it necessary to use a material which is non-dialysable in our bath water to counteract this effect and we hope to produce a fluid which is not only isotonic but also iso-osmotic. Unfortunately this is not all, for as Dr. Campbell has recently confirmed, the plasma osmotic pressure of patients with uremia is raised and, in a case recently treated, this was in the region of nine atmospheres and was reduced to nearly seven by treatment. It may be necessary to produce a fluid which is maintained at the same osmotic pressure throughout treatment.

SUMMARY

It seems that it is now mechanically possible to withdraw and return the blood without detriment to the patient. Although a rotating type of dialyser produces the maximum dialysis it is bulky and it is felt that before long a more portable type of dialyser can be achieved. Although successful cases are being recorded, further work is required to find an ideal dialysing fluid.

My thanks are due to the Medical Research Council for an expenses grant, Mrs. Adair of the Physiological Department, Cambridge University; Dr. Campbell of Messrs. May and Baker; and last, but not least, to Mr. Harris, Managing Director, and Mr. Harrison of Goddard's Garage for the painstaking care with which they have constructed the many apparatuses used in this research.

I think we have confirmed that by peritoneal dialysis urea, and presumably other toxic products, can be removed from the blood stream.

There is no doubt that clinical improvement occurs which cannot be translated into statistical terms.

We have shown that care of the fluid electrolyte balance is of the greatest importance.

When intermittent injection is used we have shown that rapid diffusion of urea occurs, reaching the level of that in the blood within two hours, and we have also shown that the concentration of urea in the wash may exceed that in the blood stream.

Before peritoneal dialysis as the treatment of uræmia can be put upon a safe basis it is necessary to settle certain questions: (a) The method of carrying out peritoneal lavage, whether by continuous perfusion or intermittent injection and withdrawal. (b) The constitution of the proper fluid for perfusion.

(a) It is my belief at present, that intermittent injection and withdrawal is better and safer than continuous perfusion. Continuous perfusion requires vast quantities of sterile fluid and the exchange goes on so rapidly that dangerous changes may occur before the laboratory estimations can indicate their presence. Disaster may be on the patient while one is waiting for laboratory results. I prefer therefore intermittent injection and withdrawal because one can call a halt for the assessment of the position between each perfusion. In continuous perfusion it is possible that the fluid may follow one track which will soon be enclosed in adherent coils of bowel and omentum, so that the contact area between the perfusing fluid and the peritoneum is very much reduced.

(b) The fluid should have the following qualities: (i) It must be a fluid permitting rapid diffusion of waste products into it. (ii) It must be a fluid which will not grossly alter the electrolyte and water balance of the extracellular fluid. (iii) It must have an osmotic pressure near that of plasma. (iv) It must be adjusted to combat acidosis and alkalosis.

We have used various solutions, the most satisfactory in our cases probably being 5% glucose in saline. William Abbott has shown by animal experimentation that a modified Hartman's solution containing glucose satisfies the criteria of removing waste products and not upsetting too grossly the extracellular fluid. Fine, Frank and Seligman use a modified Tyrode solution. The composition of these fluids has been published.

In the modern treatment of uræmia peritoneal dialysis undoubtedly has a part to play. It should only be used in cases of temporary renal suppression when there is definite hope that the kidneys will recover sufficiently to maintain life, and it must be used with the greatest care for it is a dangerous procedure. It must above all not make the patient worse. Attention must not be focused entirely upon the removal of waste products to the exclusion of maintaining the physical and chemical stability of the extracellular fluid. Neither the cardiovascular system nor the kidney should be overloaded with water.

Peritoneal dialysis is a method in its infancy. It may one day be the most potent weapon in our hands for the treatment of uræmia and it may even be extended to the relief of other toxæmias.

Dialysis of Blood for the Treatment of Uræmia. [Précis]

By E. M. DARMADY, M.R.C.P.

In the past, blood dialysis for the treatment for uræmia has largely failed. Kolff, however, overcame these difficulties, first by using a cellophane tube as a dialysing membrane and secondly by using a rotating drum to spread a small quantity of blood over a large dialysing surface. It is, of course, necessary to heparinize the patient fully and for this purpose 200 to 300 mg. of heparin are given before the treatment starts. This is backed up by running heparin into the machine whilst the dialysis is occurring. Many authorities have suggested that the treatment is unsuitable owing to the liability to bleed but it has been found that blood transfusion and protamine sulphate will antagonize the heparin adequately in the case of sudden hæmorrhage. In considering an ideal design for such a machine it is important that a free continuous flow of blood is obtained from the patient through the dialysing system and finally to the patient again. The blood is best extracted from the radial artery since veins of large calibre are insufficient to give necessary quantities of blood (fig. 1). It is important that the amount of blood which enters and leaves the machine should be controlled, since if too much blood is allowed to enter, the dialysing surface is swamped, and the blood inadequately dialysed. In my machine the pump controls the flow of blood between the patient and the dialysing tubes and thus ensures that the surface is adequately covered. I have further found that provided the inflow and outflow pumps are exactly synchronized there is no danger of shock to the patient (fig. 2). At first it was thought that it was of importance to limit the amount of blood withdrawn from the body at one time but by filling the machine with blood first this does not prove to be an obstacle. By winding the dialysing tubing round a rotating drum, it not only spreads a small quantity of blood over the dialysing surface but

also produces agitation. This ensures that a fresh sample of blood is being constantly brought to the dialysing surface. In fact, the success of agitation has enabled me to cut down the size of the drum and the dialysing surface. We have also found that by synchronizing our drums to our pumps so that 10 millilitres of blood enters the machine for each complete rotation, a better and more even film is produced which leads to better dialysis. This machine, however, is bulky and has a large number of points which have to be attended to. The bath water is not only exposed to the air, adding to the chance of becoming infected but also the dialysed products tend to build up in the water and thus slow down dialysis. This has led us to search for a machine of simpler design and we have found that by leading a cellophane tube through a machine in which there is a series of plates 1/16th inch apart a large dialysing surface can be achieved. The flow of dialysing fluid is arranged by means of a number of small tubes in the plates which allow the dialysing fluid to flow from the centre outwards in either direction. Unfortunately this machine does not at the moment produce as satisfactory dialysis as the rotating machine.

The most important of all the factors which control successful dialysis is the composition of the fluid in the dialyser. Hitherto these fluids have been of the simple electrolyte pattern, they have contained salts which are isotonic with normal blood but have added glucose

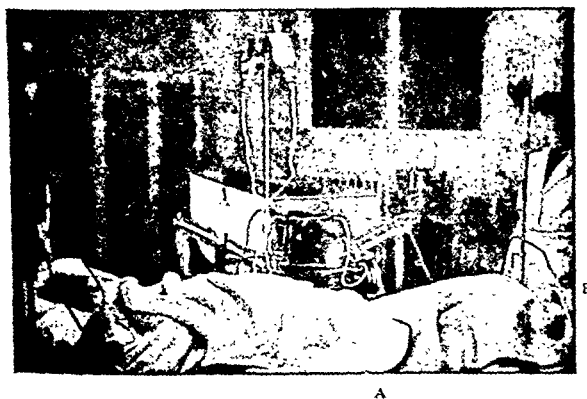


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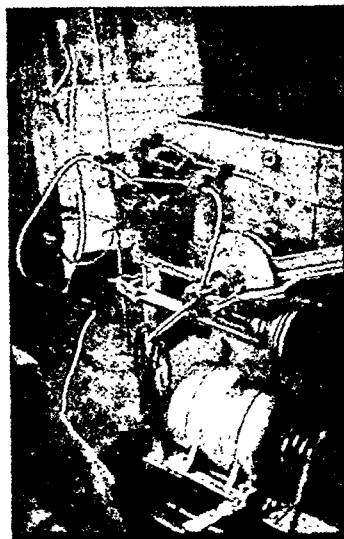


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The Artificial Kidney: Its Clinical Application in the Treatment of Traumatic Anuria

By E. G. L. BYWATERS, M.R.C.P., and A. M. JOEKES, B.M.

DURING the late war, workers at the British Post-Graduate Medical School became interested in pigment nephrosis, following burial beneath debris, which they showed to be due to muscle necrosis. Since then we have observed similar histological changes in the kidney of almost all traumatic anuria cases resulting from civilian industrial and traffic accidents, without any prolonged compression: As Barlow, Bywaters and Stead were able to show in 1944, a number of these cases excreted myohæmoglobin in the urine, derived from the necrotic muscle near the fracture sites, and we believe, therefore, that the majority of cases of traumatic anuria are due to pigment nephrosis resulting either from myolysis, e.g. vessel rupture or obstruction (Bywaters, Belsey *et al.*, 1942), muscle rupture (Barlow, Bywaters and Stead, 1944), electric shock (Fischer *et al.*, 1947), flogging (de Langen, 1946) or weight of the unconscious body (Gunther, 1940), or from hæmolysis, e.g. overheating, mismatching, myanesis (Hewer and Woolmer, 1947), Welch infection (Hill, 1946), intravenous water as in transurethral prostatectomy (Burnett *et al.*, 1947), intravenous soap solution in abortion (Weilerstein, 1944), sulphonamide hæmolysis, &c. In addition, other adjuvant factors, we believed, were probably also of importance, such as low rate of urine flow and of renal blood flow, low urinary pH and high salt concentration. It seems to us possible that proteins other than pigmented ones might also be involved in other conditions.

Now the immediate interest of all these differently produced lesions is that they affect primarily the distal convoluted tubule and they have thus been described by Lucké (1946) under the heading of "Lower Nephron Disease". If the patient can be tided over the first week, the affected epithelium is desquamated and excreted in the urine as a cellular coat to the pigment cast: regeneration with obvious mitosis from the basement membrane occurs and a diuresis sets in. If this is early enough or large enough the patient will recover and may ultimately, e.g. in five months, reach up to 100% of normal renal function. But as may be seen in fig. 1, the patient may die in uræmia despite a diuresis of even up to 2 litres daily, chiefly because this maximum output is not sufficient to offset the low concentrating power of the kidney in its early phase of recovery. The only means we had of dealing with this situation were of no great value: (a) We could depress serum potassium level (from whose cardiotoxic effects these patients seemed on occasion to die), by the injection of insulin, thus down which are responsible for uræmia by giving saline and producing generalized oedema, but this, if carried too far, is extremely dangerous since it leads to pulmonary oedema; (c) purging and sweating can only eliminate very small quantities of metabolites.

We were thus anxiously looking for some reliable method of tiding the patient over this danger period when we heard that a Dutchman had perfected an artificial kidney (Kolff and Berk, 1944). In response to our invitation, Dr. Kolff was kind enough to come over to set up and used first in October 1946. Since that time, the Kidney Unit has dialysed 12 patients, a small number compared with the number of suitable cases occurring in the Metropolitan Area. The essential details of these are listed in Table I.

TABLE I

Case No.	Diagnosis	Hours of dialysis	Blood flow ml./min.	Fall in blood urea mg./100 ml.	Grammes urea removed	Survival days
I	Bilateral hydronephrosis	1.0	10	470-?	—	3.0
II	Cortical necrosis (post-partum)	3.3	75	316-223	27.0	0.3
III	Post-traumatic anuria	4.1	86	390-211	32.1	—
IV	Hæmoglobin nephrosis	7.5	58	460-209	92.0	0.5
V	Acute glomerulonephritis	3.0	80	504-428	29.0	0.4
VI	Chronic nephritis	1.0	72	750-?	—	0
VII	Bilateral hydronephrosis	4.4	51	440-292	44.1	1.6
VIII	Post-operative anuria	4.1	76	424-264	33.1	—
IX	Aspirin suicide	3.0	58	105-59	7.5	5.0
X	Acute glomerulonephritis	2.3	50	428-307	21.0	0.2
XI	Chronic nephritis	3.7	70	400-238	65.0	0.4
XII	Bilateral hydronephrosis	3.3	80	360-178	28.7	14.0

INDICATIONS

The type of case best fitted for the artificial kidney is one in whom recovery of renal function will eventually occur, that is, one with either functional disorder or disease affecting the tubules rather than the glomeruli. Once the glomeruli are damaged, as in subacute or

chronic glomerulonephritis, polycystic disease, advanced long-standing hydronephrosis, or cortical necrosis, no restitution will occur. In uræmia of functional origin, e.g. extrarenal azotæmia or alkalosis, adequate attention to the electrolyte composition of the body should restore health, unless a calcium nephrosis has supervened, as sometimes seems to happen in alkalosis. Thus in the uncomplicated case there is seldom need to use the artificial kidney. In lower nephron disease, however, many will fail to recover spontaneously and it is these that will probably turn out to be the best indication for the use of this machine. As will be seen from the second column of Table I, only a few cases were of this type; the majority, some of them obscure in nature on first admission, turned out ultimately to be cases of glomerulonephritis. These were dialysed, sometimes even without full knowledge of the

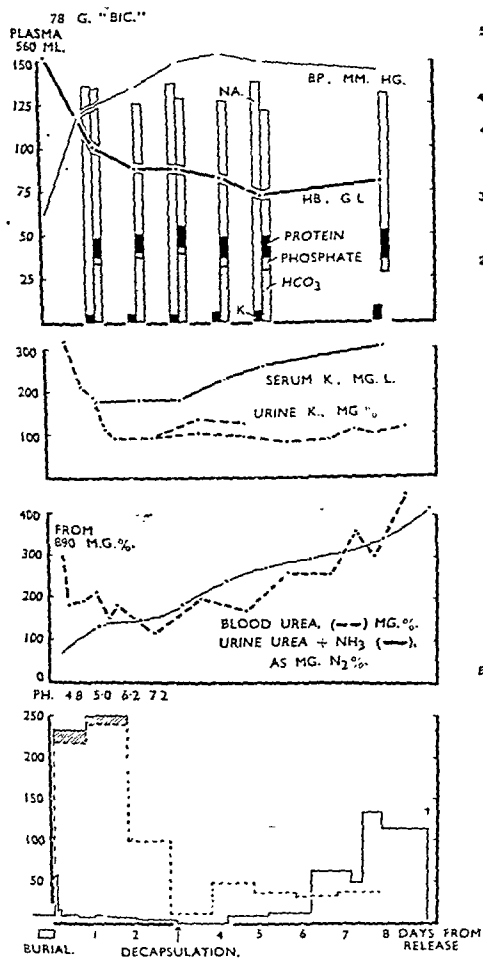


FIG. 1.—Case of ischemic muscle necrosis due to crush injury, developing anuria despite intake of 150 ml. per hour over three days. Decapsulation produced no increase in urine output. A spontaneous diuresis developed on the seventh day, reaching 2½ litres per day with continued rise of blood-urea level, and death from uræmia on the ninth day. Note that urea concentration runs parallel to blood level, and thus shows no sign of return in concentrating ability.

diagnosis, because the prognosis was believed to be otherwise fatal. The same holds for the cases of hydronephrosis due to inoperable carcinoma; they were cases whose condition before dialysis was too bad even for pyelostomy to be carried out. It will be seen that two cases were dialysed for less than an hour; one of these was our first case in whom incannulation was unsatisfactory, producing such a very low rate of arterial inflow (10 ml. per minute) that dialysis was discontinued; the other was moribund at the beginning of dialysis, with a blood urea of 750 mg.%, and died in one hour.

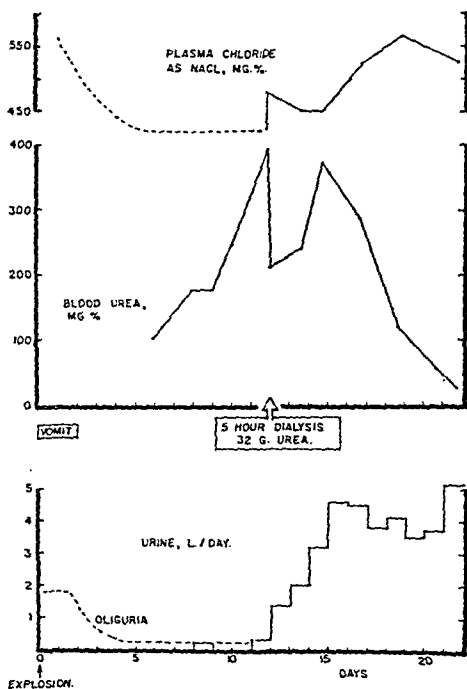


FIG. 2 (Case III).—Development of oliguria following an explosion, with blood urea reaching 390 mg.%. A five-hour dialysis (4.1 effective hours at 86 ml. per minute), reduced blood urea to 211 mg.%, and removed 32 grammes urea. Following dialysis, note secondary rise in blood urea which is overtaken by diuresis.

SURVIVAL

Of the remaining 10, 2 have survived, and, we believe, probably because of the dialysis rather than in spite of it, although this is difficult to substantiate except by statistical means on a larger series of cases.

CASE III.—A male, aged 31, had been knocked down by the explosion of a car battery and possibly rendered unconscious for a short period. He walked home having no obvious injury. The next two days he vomited repeatedly; it was not until the fourth day that he became oliguric and on the seventh day he attended the Outpatient Department at University College Hospital complaining of "urine in the breath" and oliguria. The next day he was admitted with a blood urea of 102 mg.%. As the oliguria persisted despite 5 litres of intravenous sulphate, and the blood urea rose to 246 mg.%, a right splanchnic block was done and a cystoscopy performed at which a clear efflux was seen from the right and none from the left kidney. He was therefore transferred to the British Post-Graduate Medical School on the twelfth day (blood urea 390 mg.%, CO_2 (C.P.) 44 vols.%, chloride as NaCl 419 mg.%, hæmoglobin 88%, Haden 13.6 grammes%). Urine, pH 8.6, albumin 40 mg.%, urea 526 mg.%, ammonia 54 mg.%, chloride 260 mg.%. After dialysis for five hours with the removal of 32 grammes of urea, his condition improved, but oliguria was still present (*see fig. 2*) with low urea content, 565 mg.% and a still lower chloride level, 120 mg.%, despite a rise in plasma-chloride level to 476 mg.%. It was not until the third day after dialysis that urine output reached a satisfactory level with an increase in urea concentration to 1040 mg.% and following this, with chloride by mouth, the plasma chloride rose. Thereafter except for a right perinephric abscess, and root paralysis L 2, 3 and 4, recovery was uninterrupted. Follow-up showed a normal intravenous pyelogram and maximum sp. gr. 1.024.

CASE VIII.—A female, aged 52, was admitted to St. John's Hospital, Lewisham, for removal of gall-stone.

Examination.—B.P. 135/85. Urine: no albumin, sp. gr. 1.020.

Operation.—Following myanesin injection, cholecystectomy was performed with the removal of a stone impacted at the junction of cystic and common duct. Appendix was removed and right kidney was found to be normal. The blood urea rose and remained at a very high level despite a urine output of about a litre per day (*see fig. 3*), and some vomiting. Urine studies after operation showed albuminuria,

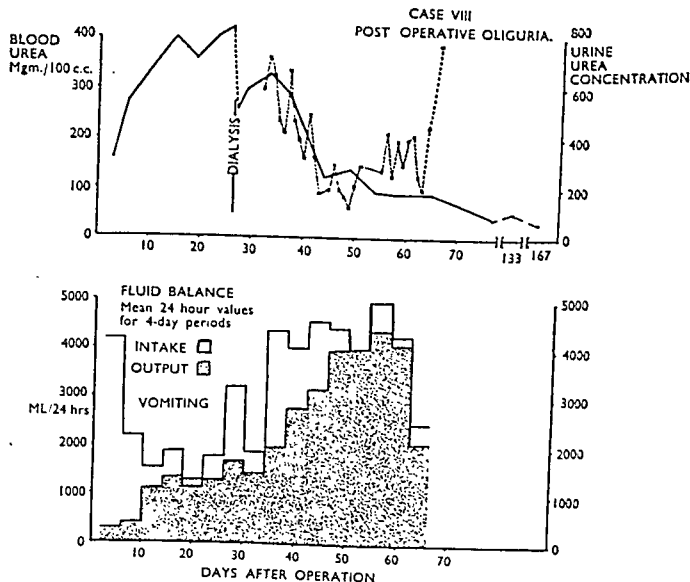


FIG. 3 (Case VIII).—Chart showing uræmia, following cholecystectomy: dialysis removed 33 grammes urea and blood urea fell from 424 to 264 mg.%, with gradual recovery on a high fluid intake, and a later improvement of concentrating ability.

many granular casts, a specific gravity 1.010–1.014, chloride content (as NaCl) 200 mg. (third and fifteenth post-operative day), urea 600 mg.% (fifteenth day) and 100 mg.% (twenty-third day). Blood studies showed hæmoglobin 10.2 grammes%, plasma protein 5 grammes% (sixth day), chloride as NaCl 370 mg.%, CO_2 (C.P.) 47.6 vols.% (seventeenth day), sodium 238 mg.%, phosphate 10.2 mg.%, creatinine 10.7 mg.% (twenty-third day).

¹Due probably to sulphate retention.

On admission to Hammersmith Hospital (twenty-sixth post-operative day) she was mentally confused, no oedema, no raised venous pressure, B.P. 155/90, CO₂ (C.P.) 38.5 vols.%, chloride as NaCl 468 mg.%, blood urea 424 mg.%, sodium 334 mg.%, potassium 20.5 mg.%. She was dialysed for 4.1 hours and given four bottles of blood, with the removal of 33 grammes of urea and a reduction of blood urea to 264 mg.%, rise of chloride to 548 mg.% and of CO₂ (C.P.) to 45 ml.%.

In the eight days following admission and dialysis almost anything given by mouth was vomited; and despite a large parenteral intake blood urea rose and urine output remained stationary at about 1.2 to 1.5 litres/day. On the thirty-fifth post-operative day intravenous therapy started a gradual increase in output (which thereafter rose to 4 litres/day) and, as may be seen from the chart, a gradual rise in urine urea concentration occurred to 400 mg.% despite this large diuresis and the continuously falling blood level, thus attesting a renal recovery.

Follow-up studies have shown no abnormality by pyelography, and function has gradually returned towards normal (Table II).

TABLE II.—RENAL FUNCTIONAL RECOVERY (CASE VIII)
Days post-op. Clearance figures

37	Glomerular filtration (mannitol)	4.2 ml./min.
	Renal plasma flow (PAH)	10.4 ml./min.
68	Glomerular filtration (mannitol)	20.0 ml./min.
	Renal plasma flow (PAH)	130.0 ml./min.
77	Urea clearance	26% of normal
134	Creatinine clearance	20.0 ml./min.
	Urea clearance	39% of normal
168	I.V.P. showed fairly good concentration both kidneys, with normal outline	
291	Creatinine clearance	168.0 ml./min.
	Renal plasma flow	452.0 ml./min.

Comment.—This was probably a case of pigment nephrosis due to myanesin hæmolytic. The available data was insufficient to support this or any other ætiological hypothesis.

Of the remaining 8, all died at varying intervals, up to fourteen days. In some cases this was due to the inevitably fatal character of the disease, as in several with severe and advanced glomerulonephritis; in some, it was due to the dangerously labile cardiovascular state, and this was particularly noticeable in the cases with acute glomerulonephritis where it seemed very easy to overload. In one case where it seemed possible that we might be successful, in that the patient had a pigment nephrosis, conditions antecedent to his admission tipped the scales against his recovery:

CASE IV.—A male, aged 36, after some bleeding following herniorrhaphy was transfused, at another hospital, with 500 ml. of incorrectly matched blood. Within forty-five minutes, backache, rigors and nausea developed (B.P. 170/110). 120 ml. of urine containing free hæmoglobin was withdrawn two hours later, and over the next day he became oliguric (120 ml./day), jaundiced, blood urea 106 mg.% despite lactate (2 litres), 5% glucose saline (2 litres), alkali sodium sulphate and caffeine. A high spinal anæsthetic was given with no result.

On the third day 30 ml. urine only was passed, with no casts but containing methæmoglobin. B.P. 170/100, hæmoglobin 10.2 grammes%, urea 110 mg.%. Glucose saline (4 litres) and sulphate (1 litre) were given, bilateral renal decapsulation was performed and peritoneal washouts were started through a catheter (1.1 litre in twenty-four hours, urea content 100 mg.%).

Thereafter blood urea rose steadily (see fig. 4). Dyspnœa, venous congestion and oedema developed due to overload and the urine output over the fourth and fifth days averaged 120 ml./day, hæmoglobin 7.6 grammes%, CO₂ (C.P.) 50 ml.%, Na 321 mg.%, chloride as NaCl 351 mg.% (fourth day). Another attempt at peritoneal dialysis was made on the sixteenth day without improvement, despite morphia, atropine, paraldehyde, caffeine, sodium bicarbonate, potassium citrate, magnesium sulphate, ephedrine, benzedrine, ascorbic acid, ferrous sulphate, anahæmin, phenobarbitone, sodium sulphate, sodium lactate, sucrose, glucose, saline, Hartman's solution, blood, plasma, and penicillin.

He was admitted to the British Post-Graduate Medical School on the eighteenth day comatose, grossly oedematous, and very heavily infected at all three incisions with pyocyaneus. B.P. 200 mm.Hg. The patient was dialysed for 7.5 hours and given four bottles of blood with the removal of 92 grammes urea and fall of blood level from 560 mg.% on entry to 209 mg.%.

He came out of coma and became rational, asking for a cup of tea and conversing with his neighbour in the ward. Signs of pulmonary oedema evident on entry had receded. Six hours later, however, his condition suddenly worsened with dyspnœa, loss of consciousness and signs of pulmonary oedema, death occurring twelve hours after the end of dialysis. Post mortem (peritoneal fluid urea 350 mg.%) confirmed the pulmonary congestion, widespread pyocyaneus infection and pigment nephrosis.

Comment.—Gross overloading with fluid and pyocyaneus infection seemed to contribute to this end, after a very successful dialysis both from the view of the blood-urea level and the systemic fluid overload. It seemed also possible that glucose deposition as glycogen might sufficiently alter electrolyte balance to upset the established equilibrium.

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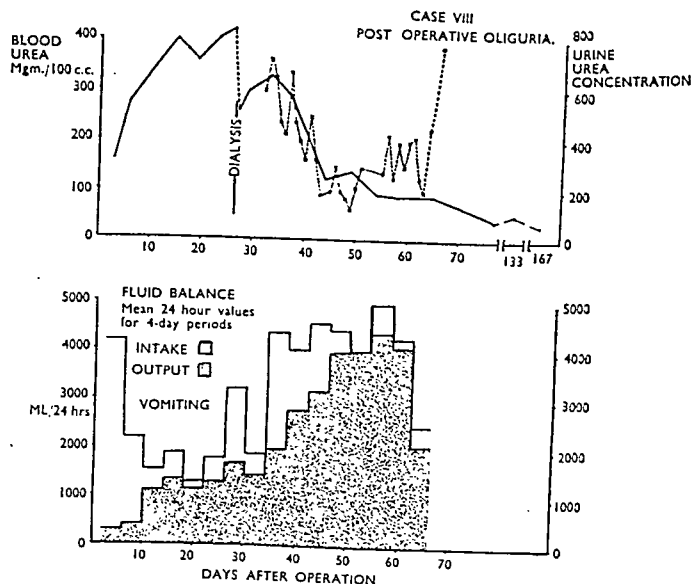


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¹Due probably to sulphate retention.

HEMORRHAGE

However, one death at least was probably related to therapy, a patient with uræmia due to acute glomerulonephritis (Case X). After a successful dialysis removing 21 grammes urea and bringing blood level from 428 to 307 mg.%, he suddenly developed an acute headache three hours after his return to the ward and died with subdural hæmorrhage; although purpura does occur spontaneously in nephritis it seems probable that heparinization played a considerable role here. This complication of heparinization does not seem to have occurred in any of Kolff's cases (Kolff, 1947) and we have had no serious trouble with bleeding in other cases. The incannulation wounds do not bleed if large vessels are secured and adequate time for clotting is allowed before heparinization. Further, we have had no bleeding from a quite recently separated placental site (Case II) or from recent operation wounds (Case IV). It has now been found possible to reduce the total heparin needed for a normal-sized adult from 1 gramme to 500 mg. without clotting in the machine. Protamine sulphate will bring coagulation time back to normal in a few minutes, but it is necessary to give enough to neutralize all the heparin (Table III).

TABLE III

1 gramme protamine sulphate	=	1.5 grammes heparin
Heparin (Boots) 50 mg. in 5 ml.	=	5,000 Toronto units
Heparin (Swedish) 50 mg. in 1 ml.	=	5,000 internat. units
Protamine Sulphate (Swedish) 5 ml. of 1% solution	=	50 mg. protamine
Hence 5 ml. protamine sulphate solution	=	75 mg. heparin

OTHER TECHNICAL DETAILS

While we have made no major alteration in the set-up described by Kolff (1947), we have introduced several modifications which we think to be improvements. Fig. 5 shows a modification of the circuit which avoids the excessive pressures under which blood was formerly pumped from the machine into the patient's vein, often measuring as high as 300 mm.Hg, and partly responsible, we thought, for venous spasma. The pump drives blood from the venous end of the machine into a simple gravity-feed burette; this also allows for a further modification recently introduced by Joekes and Bull where, instead of continuous flow, a strictly measure-for-measure bleeding and replacement is performed; this is of especial value in those patients with labile circulations, such as in acute glomerulonephritis or severe chronic anæmia where overloading or overbleeding is particularly dangerous. Even with measure-for-measure venous replacement of arterial outflow, however, the osmotic forces in the bath may produce an increase or a decrease in body fluid and circulating volume. Of great value in difficult cases is the introduction of a catheter into the right auricle and the return of blood through this. With this in situ, regular readings can be made of right auricular pressure and of cardiac output, so that early warning of tendencies to overload or exsanguinate is available. An internal catheter diameter of 2 mm. is necessary to maintain an approximate rate of flow of 100 ml./min. at a pressure of 100 cm. H.O.

We have not found it essential to change the bath water during the course of even an eight-hour dialysis since the arterial level of urea, &c., is dependent on an equilibrium between the urea output of intracellular- (45% of body-weight) and interstitial-fluid compartments and the bath-water urea uptake; its rate of fall seems to be little affected by rise of bath-water concentration as high even as 50% of the blood level (*see* fig. 6). The composition of the dialysing fluid we have used is as shown in Table IV. In severely œdematous patients we

TABLE IV.—COMPOSITION OF BATH WATER

Constituents		Concentration per 100 ml.	
600 grammes NaCl	..	Calcium	.. 3 mg.
1,500 grammes Glucose	..	Glucose	.. 1,500 mg.
200 grammes NaHCO ₃	..	Chloride (as NaCl)	630 mg.
40 grammes KCl	..	Sodium	.. 290 mg.
100 litres tap water	..	CO ₂ (C.P.)*	.. 54 ml.
		Potassium..	.. 20 mg.

* Combining Power

have used 2 grammes% glucose, but as in the body this is stored as glycogen, the resultant electrolyte shifts might possibly result in a potassium deficiency, as we have seen in insulin-treated diabetics. The level of glucose in the patient's blood reaches only as high as 600 to 700 mg.% although the post-kidney blood may be as high as 1,500 mg.%. We have, therefore, used a potassium concentration at the upper end of normality (Note that 20 mg.% in serum is 21.5 mg.% in serum-water). It would probably be better to use some macromolecular substance not diffusible through cellophane, such as dextran, gum acacia, or even plasma protein, but we have not yet been able to do this.

Other types of death were also associated with conditions antecedent to dialysis; thus Case V was cyanosed before and became almost asphyxiated during the dialysis due to a widespread bilateral bronchopneumonia: the blood in the coils of cellophane was dark blue in colour.

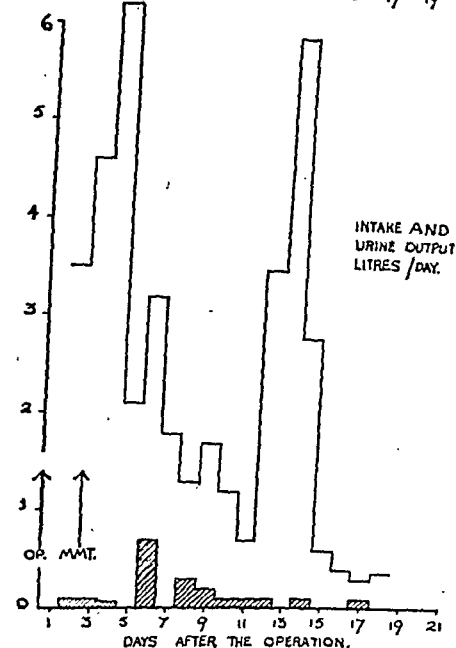
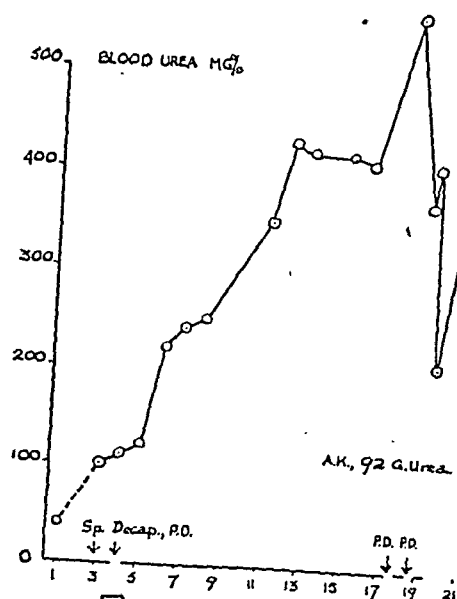


FIG. 4 (Case IV).—Chart showing development of uræmia, following mismatched transfusion. Following failure of spinal anæsthesia (Sp.) peritoneal dialysis (P.D.) and decapsulation, dialysis on the artificial kidney for seven and a half hours removed 92 grammes urea, but death occurred twelve hours after, from a return of pulmonary oedema and widespread sepsis.

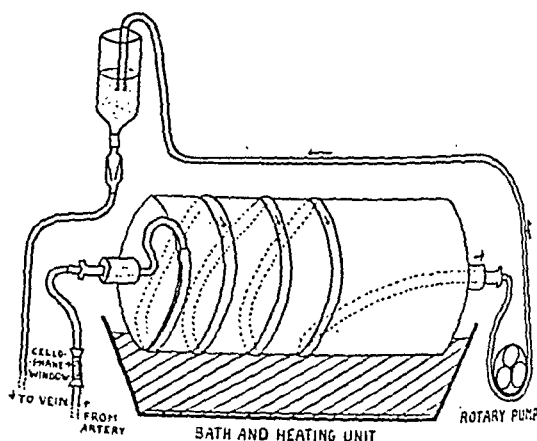


FIG. 5.—Modification of Kolff's artificial kidney showing return of blood to gravity-feed burette following dialysis.

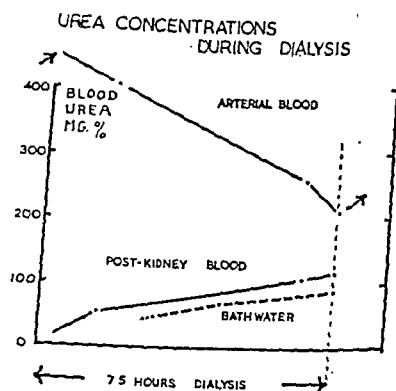


FIG. 6 (Case IV).—Showing continued fall of arterial urea levels with decrease of arteriovenous concentration gradients due to rise in level of bath-water concentration. Note that concentration of urea in the venous end of the kidney runs parallel to and just slightly above the bath-water concentration.

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The virulence of an organism is based chiefly upon its invasiveness and its toxigenicity and the staphylococcus provides an excellent example of the utilization of both these mechanisms and of their interaction. A number of metabolites concerned in virulence are known and have been extensively investigated. Of these the available evidence suggests that α toxin and the leucocidin of Pantón and Valentine (1932) are major toxic factors, that coagulase is a major factor in the initial stages of tissue invasion and that fibrinolysin and hyaluronidase may possibly help to determine the clinical type of infection. The β toxin seems to be of little importance in human infection but may play a role in infections of lower animals. The enterotoxin produced by some strains is, of course, a cause of food poisoning but is not concerned with infection in the true sense of the term. Evidence in support of these statements has been provided by four different methods of investigation.

(1) *Correlation studies.*—Several investigators have attempted to analyse the virulence factors of the staphylococcus by isolating numbers of strains and by studying the correlations between their production of various metabolites and the clinical evidence of their pathogenicity or non-pathogenicity. All workers agree that the closest correlation occurs with staphylocoagulase. For example, the investigation by Schwabacher *et al.* (1945) of over 800 strains isolated from human sources indicates that in order to be pathogenic a staphylococcus must be able to produce coagulase. The converse, that power to form coagulase makes an organism pathogenic, does not, however, necessarily follow. Additional factors may be essential. Thus these same workers found that over 98% of coagulase-positive strains isolated from definite staphylococcal infections produced also α toxin and hyaluronidase. The same combination of metabolic activities was shown by about 90% of coagulase-positive staphylococci obtained from persons with no sign of infection. On the other hand, coagulase-negative strains, whether isolated from wounds or from healthy persons, were never found to produce either α toxin or hyaluronidase. Our own unpublished results with human strains are in agreement as far as coagulase and α toxin are concerned, suggesting that both these factors may be essential in the infective process in human beings. In lower animals the position may be different. H. W. Smith (1947) found a high degree of correlation between the coagulase, β toxin and fibrinolysin production of staphylococci from animal infections and when his figures are compared with those we obtained with human strains it appears that for some animal species β toxin may replace α toxin as the important toxigenic virulence factor. The possible significance of leucocidin emerges from the work of Valentine and Butler (1939) who suggest that it may largely determine the type and severity of human infections consequent upon tissue invasion by a pathogenic staphylococcus.

Correlation studies, however, have very definite limitations and other research methods are necessary to elucidate the modes of action of the various factors and their interaction.

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The patient is, if time permits, premedicated with amidopyrine (0.6 grammes six-hourly for twenty-four hours) to guard against rigors. These are probably due to bacterial pyrogen produced on moist rubber tubing allowed (after vigorous cleaning in soda, hydrochloric acid and tap water) to lie around for an hour before autoclaving; this is a point not usually appreciated, but one very difficult always to eliminate. Sedation is accomplished with pentothal 0.2 gramme, nembutal or sodium gardenal 3 grammes repeated as necessary. Penicillin is given as a routine, and calcium gluconate injections are necessary since the bath water contains only such small amount of calcium as is contributed by the tap water (and varies thus from place to place). We have also added to the circulating blood such substances as thiamine and ascorbic acid, since such substances may be lost into the bath water. The body store of various other "threshold" substances, normally reabsorbed by the kidney, such as amino-acids, may also become depleted, but we have not yet been able to recognize any such effects clinically.

In the after-period we endeavour to maintain an intake of 2,000 calories, since various people, including, recently, Professor Borst of Amsterdam, have emphasized the nitrogen-sparing powers of a high calorie intake. He gives a mixture of 200 grammes butter and 200 grammes sugar daily, a teaspoonful of which, given iced, is quite palatable; 400 grammes, however, is distinctly tedious, our patients tell us, however disguised, and it needs a patient and persuasive nurse and a co-operative and non-vomiting patient to take it. With such an intake, body protein, normally broken down on low calorie intakes to provide calories, is spared; instead of producing 10 grammes N_2 /day (that is, 20 grammes urea and equivalent to a daily blood urea rise of 40 mg. % in a 65 kg. man or a urine output of 2 litres at the usual maximal pathological urea concentration of 1 gramme %) the body produces a mere 2 grammes N_2 (equivalent to 4 grammes urea). This means that a patient with no kidneys should last five times as long, since the substances producing uræmic death such as potassium, &c., come almost all from endogenous protein breakdown. We had also thought to increase tubular regeneration with testosterone, and have given it, but have had no chance to evaluate results. Theoretically it should be of value in association with a protein-sparing diet.

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While the clinical value of this new weapon will always be its life-saving capacity, its experimental use in animals will be intensely interesting because of one's ability with it to alter the whole internal environment of the body cells at will. There is obviously room for a great deal of improvement; Alwall's dialyser (1947) seems a step in the right direction. We have a great deal more to learn about its effective operation and about its usefulness relative to peritoneal dialysis and dietary measures.

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Dr. V. D. Allison gave a résumé of recent work on the serological typing of *Staph. pyogenes* and described the development of bacteriophage typing (Fisk, 1942, and Wilson and Atkinson, 1945). The properties of the phages used, and the technique of typing were shortly described.

The application of serological and bacteriophage typing to the investigation of outbreaks of staphylococcal infection has shown that there is a definite correlation between the two methods. Outbreaks investigated included pemphigus neonatorum in maternity units and nursing-homes, mastitis among mothers in maternity units, food-poisoning due to staphylococcal enterotoxin; and strains from a series of cases of sycosis barbæ were also investigated serologically by Hobbs, Carruthers and Gough (1947).

Much new information on the epidemiology of staphylococcal infections has been gained by the investigation of pemphigus neonatorum (Allison and Hobbs, 1947).

Twenty-three outbreaks of staphylococcal food-poisoning were investigated over a period of two years, and it appeared as though certain serological and phage types were particularly liable to produce enterotoxin and cause epidemics under suitable conditions. The importance of the nose as the ultimate reservoir of *Staph. pyogenes* was stressed, but the skin and especially septic abrasions and cuts, and even healthy-looking cuts, were frequently implicated as breeding grounds for infective strains of the organisms.

Investigation of strains from cases of sycosis barbæ showed the importance of treating the noses of carriers of staphylococci concurrently with the infection in order to prevent relapse after apparent cure.

The lessons to be learnt from the investigation were shortly discussed and suggestions were made for the improvement of techniques in infant nurseries, hospital wards and the hygienic handling, or avoidance of handling, of food. The ubiquity of the staphylococcus renders the prevention and control of infections caused by it a formidable problem.

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Dr. A. McDiarmid: *Enzootic staphylococcal infection in young lambs associated with tick-bite*.—Staphylococcal infections occur in practically all the domestic animals and birds, but most of these cases are sporadic, rarely fatal, and of little importance economically. There are, however, exceptions, such as mastitis in cattle and sheep, and I shall briefly discuss yet another disease caused by *Staphylococcus aureus* which is responsible for much death and debility in young lambs on hill farms throughout Britain. This infection differs in some interesting ways from the usual sporadic type of staphylococcal infection and is now recognized as a specific disease, enzootic in distribution with a definite age-incidence, and invariably associated with the presence of the common sheep tick *Ixodes ricinus* L. Thus it has several features of considerable interest to those engaged in the study of the epidemiology of staphylococcal infections.

As long ago as 1894, McFadyean, described a condition in sheep in Northumberland caused by a slightly chromogenic micrococcus; he named this condition pyæmic spinal meningitis and attempted to transmit the disease, by inoculating cultures subcutaneously into experimental sheep. These attempts were unsuccessful, because, although local abscesses appeared at the inoculation sites, no pyæmia developed. Stewart and Ponsford (1937) confirmed these observations and suggested that the disease was responsible for the deaths of many young lambs and subsequently a survey by Taylor, Holman and Gordon (1941) showed that the incidence of the infection in dead lambs brought for examination from tick-infested farms in Perthshire, was 29%.

Practically any breed of sheep can be affected provided the environment conditions are suitable, and infection must be contracted soon after birth as pyæmic cases are generally observed in lambs about a fortnight to one month of age. On hill farms, lambs, even a day old may harbour large numbers of ticks and thus the opportunity for early infection can readily be appreciated. The sites of tick-bite are usually inflamed and small abscesses may be present from which *Staphylococcus aureus* can be isolated. The causal agent may also be recovered from the heart blood of very young tick-infested lambs in which no visible abscesses are present and these constitute true septicæmic cases (McDiarmid, 1946a). Pyæmia, however, is the form of the infection most generally recognized and abscesses may be present in almost any situation in the body. The pressure of an abscess in the vicinity of the central nervous system may produce impairment of gait or even complete paralysis, depending on the situation of the lesion and thus, clinically, these cases may frequently be confused with true louping-ill, the cause of which is a filtrable virus.

One of the difficulties of assessing the true economic importance of the disease is its

staphylococcal investigations because of the ubiquity of the microbe and the protean nature of the lesions it may evoke. Nevertheless such reports as are available indicate that a antitoxic immunity is of importance in conferring some degree of increased resistance to infection (Parish *et al.*, 1934). Unfortunately some of the virulence factors like coagulase are non-antigenic but immunization trials with leucocidin might yield information of value.

(3) *In vitro* studies.—Certain activities of the virulence factors, though interesting, can have no significance in infection. For example, a toxin lyses rabbit erythrocytes but not human erythrocytes. This should make us cautious about attributing pathogenic significance to factors such as fibrinolysin and hyaluronidase because of their *in vitro* activity. Indeed the work of Evans with *Cl. welchii* goes to show that any influence these substances may have in experimental gas gangrene infection is so overshadowed by the toxic factor as to be negligible. Phagocytosis, however, is so well established as the first line of defence of the host after invasion of tissues has occurred that any anti-phagocytic activity of a staphylococcal metabolite is probably significant. Such activity is readily demonstrable *in vitro* in the cases of leucocidin and coagulase. Hale and I were able to show that the coagulase activity in this respect is specific against staphylococci so that other species of bacteria incorporated in the test mixtures are taken up by phagocytes just as readily as if no coagulase were present (Hale and Smith, 1945). This indicates that, unlike leucocidin, the action of the coagulase is upon the microbes and not upon the phagocytic cell. In other words, coagulase protects staphylococci against ingestion by phagocytes. *In vitro* experiments with plasmas of different animal species have given an inkling that coagulase may also be concerned in the host specificities of different strains of staphylococci. It now seems fairly certain that there are several different coagulases with different ranges of activity against the plasmas of various animals and a wide field for investigation by *in vitro* techniques is thus opened up.

(4) *Animal infection experiments*.—The importance of a toxin has been clearly demonstrated by two types of experiment: (1) Direct demonstration of its toxic effects, e.g. production of skin necrosis by intracutaneous inoculation of guinea-pigs and the lethal effect of intravenous inoculation of rabbits. (2) Immunization of animals with toxoid and toxin followed by the inoculation of living staphylococci. The second type of experiment has shown that a high level of antitoxic immunity may suffice to protect against experimental infection, but often the protection is incomplete so that in spite of modification of the course of infection the animals eventually succumb. This is in keeping with the view that in the case of staphylococci no single virulence factor is of predominant importance.

This line of investigation is obviously worth extending to other factors like leucocidin, hyaluronidase and fibrinolysin. Coagulase, however, is neither directly toxic nor antigenic so that a more indirect approach has been necessary. A comparison of strains capable of coagulating guinea-pig plasma with those not able to do so showed that the former were much more virulent for the guinea-pig when inoculated by either the intracardiac or intratesticular route. Again pre-treatment of staphylococci with a coagulable plasma rendered them more infective for mice, a species which is relatively insusceptible to staphylococcal infections, probably because mouse plasma is non-coagulable by the staphylocoagulase of nearly all strains. The analysis of the role of coagulase in infection has been attempted by many modifications of such kinds of animal experiments and all go to confirm its importance (Smith, Hale and Smith, 1947).

To summarize: I suggest as a basis for discussion that in the case of staphylococci there is no one all-important infectivity factor such as the toxin of type A, *Cl. welchii*. Coagulase and a toxin are certainly major factors in human infections but other toxins, like the β toxin, may be found to take the place of a toxin in the infection of other animal species. The indications are that coagulase helps the organism to initiate infection whilst toxins come into play subsequently. Leucocidin is also important but whether it is essential in the genesis of an infection we do not know; possibly its chief importance is in determining the severity and type of the disease once an infection has been established. Fibrinolysin and hyaluronidase may also play a part in the development of the infective process but the demonstration of their *in vitro* activities does not suffice to establish their *in vivo* significance.

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JOINT DISCUSSION No. 2

Sections of Medicine, Radiology and Surgery

[February 24, 1948]

Chairman—Sir ALUN ROWLANDS, K.B.E., F.R.C.P.
(Vice-President of the Section of Medicine)

DISCUSSION ON CHRONIC DISEASES OF THE PERICARDIUM

Dr. B. T. Parsons-Smith: The diagnosis and rational treatment of chronic pericarditis not only includes physiological and clinical considerations but also a clear conception of the various ætiological factors known to be responsible for the disease and for the morbid anatomy secondary thereto. The reason for this is not far to seek. Chronic pericarditis is not a single or a constant condition. It comprises a number of different processes and a variety of stages which are of different significance and which call for totally different kinds of management. The disease occurs as an intercurrent complication in cases of chronic carditis; its tuberculous origin has been amply confirmed, as has also its intimate relationship to polyserositis; additional causes deserving of passing mention include chronic renal disease and diabetes in their final stages, coronary disease and malignant disease, the latter by direct spread from viscera in the neighbourhood of the heart or by blood-borne metastases. Two well-recognized varieties of chronic pericarditis, the adhesive and the constrictive, although combined in a certain proportion of cases, are deserving of separate consideration. In the majority of cases, rheumatism or tuberculosis constitutes the pathological background of the adhesive group. If rheumatic the condition may be singularly elusive from the diagnostic point of view owing to the fact that the clinical indications of the pericardial affection are frequently masked by signs of co-existing valvular and myocardial disease. Although, however, it is common knowledge that, with extensive internal adhesions, and complete obliteration of the sac, localizing signs are, as a rule, entirely lacking, it is generally agreed that external adhesions are capable of clinical recognition. These latter are instrumental in the formation of attachments from the pericardium to certain of the adjacent structures including the ribs, the sternum, the lungs, the diaphragm and the spine, also for the development of indurative changes in the mediastinum. The diagnosis of adherent pericardium involves an extensive clinical examination of which the outstanding features in all cases should be the routine radiological investigation. The physical signs of agreed diagnostic value are as follows:

(1) Pericardial friction sounds and triple heart rhythm, the third sound of the latter being that recently described by Professor C. Lian as “the late systolic pleuro-pericardial snap”.

(2) A persistently raised venous pressure with evidence of stasis in the systemic and the portal circuits.

(3) Varying degrees of peripheral œdema, the distribution of which may include

co-existence with other infections. Frequently a young lamb may be affected with two or more diseases at the same time; louping-ill often exists along with pyæmia and tick-borne fever may even be present in the same lamb. Lamb dysentery and pulpy kidney disease may also co-exist with staphylococcal infection, and on a hill farm, unless one carries out a very detailed bacteriological examination, it is impossible to decide which factor may be responsible for the death of the lamb.

The precise way in which the tick acts in the causation of the disease is not yet fully understood. Tick-bite appears to be essential for the development of the disease because the infection is only seen in tick-infested lambs and the staphylococci isolated from the small abscesses at the site of tick-bite are apparently the same as those recovered from the internal lesions. Moreover staphylococcal abscesses rarely appear at wounds caused by surgical interference such as docking or castration or even at the umbilicus, which is a favourite entrance for other pathogenic organisms. It is possible that the tick may act merely in a passive way, creating a small punctured wound and thereby carrying in staphylococci which the tick has picked up during its wanderings on the surface of the body. Owing to the anticoagulating nature of the tick's secretions the organisms have every opportunity of gaining immediate access to the blood-stream instead of being arrested at the original site of entry. *Staphylococcus aureus*, incidentally, can be recovered from the skin of normal ewes and lambs and these strains are potential pathogens, resembling in every way the strains recovered from actual pyæmic cases. The organism has also been recovered from engorged ticks attached to pyæmic lambs, but not from ticks obtained from normal lambs (McDiarmid, 1944). Foggie (1947) has carried on this work and apparently does not believe the tick can carry the infection through the moult and then transmit the infection to another lamb. The evidence, so far, all points to the tick as a mechanical aid to the development of infection rather than as a true vector.

As regards the bacteriology of this condition, many strains of staphylococci have been examined. Most of the strains are coagulase-positive and produce septicæmia or pyæmia, according to the dosage, when injected intravenously in mice, guinea-pigs and young lambs (McDiarmid, 1946*b*, *c*, and 1948). They give rise to bright orange pigmentation when grown on milk agar and produce α and β toxins. Their biochemical reactions are, with rare exceptions, identical, and cross agglutination tests show a considerable degree of serological relationship. Recently Smith (1947) by phage typing, has confirmed the close relationship between strains recovered from pyæmic cases.

In order to reduce the rate of infection on tick-infested farms, various preventive methods have been tried. The best method of attack is to reduce the tick population and render the lambs immune to tick infestation over as long a period as possible. Progress towards this end is being made and D.D.T. dips should prove to be of considerable value. In the second place, can the lamb be given a passive immunity from the ewe at birth? Active immunity is impracticable because of the early age-incidence of the disease. In Scotland we have attempted to hyperimmunize ewes with toxoid, prior to parturition. The antitoxin content of the ewe's colostrum was high at parturition and consequently the blood of the lamb after sucking showed a high level of antibody comparable to that of the mother's blood, but this high antitoxin content in no way protected the lamb against a small test dose of the staphylococcus.

Penicillin therapy could, perhaps, be used either alone or in conjunction with antitoxin, as these strains are fully sensitive to this antibiotic, but again the practical difficulties in dealing with conditions prevailing on a hill sheep farm could hardly be overcome. Diagnosis would be invariably too late and mechanical impairment of function would have ensued before treatment could be applied.

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nausea and an irritating cough; the heart was found to be considerably enlarged, the apex impulse could not be seen or felt, the sounds were faint, the pulse small and rapid (110), the respiratory rate 22, the temperature intermittent and rising (100° – 101°) and the blood-pressure 110/80; there was a loud friction rub over the whole præcordium of maximum intensity at the base; the cardiogram showed low voltage curves with inverted T waves in leads I, II, IVR and IVF and the X-ray showed the typical shadow of a large pericardial effusion; the patient's progress appeared to fall into three phases:

- (1) The phase of increasing effusion with hypotension and congestive failure.
- (2) The phase of decreasing effusion with a steady rise of blood-pressure and temporary recovery.
- (3) The phase of deterioration characterized by a rising pulse-rate, a falling blood-pressure, a diminished pulse-pressure, pulsus paradoxus, congestive failure with gross œdema and an increasing irregularity of the cardiac shadow by X-ray, suggestive of progressive thickening of the pericardium. The authors suggested that the apparent improvement during the second phase of the man's illness was illusory, the relief following the absorption of the pericardial exudate being not yet offset by the hampering effect of the gradual thickening of the visceral pericardium on the action of the heart.

It remains to mention constrictive pericarditis, a condition characterized pathologically by widespread indurative disease of the pericardium, the effect of which is to restrict the range of cardiac motility, limiting more particularly the filling capacity of the ventricles and so diminishing the volume of their output per beat. Elevation of the venous pressure is a further development of considerable significance in constrictive pericarditis, being probably the outstanding cause of the œdema and the serous effusions which frequently characterize the disease. Lyons and Burwell (1946) investigated the effect of raised venous pressure upon cardiac filling and cardiac output in patients with constrictive pericarditis and they compared their results with the reactions of a normal heart in which the natural response to a rise in venous inflow is an increase in its filling and output capacities. They tested the effects in patients with constrictive pericarditis both of increasing and of decreasing the venous pressure by intravenous infusions of glucose and saline and by phlebotomy respectively, and their circulatory measurements in these circumstances excluded any variation in the volume of the cardiac output. They concluded that, by reason of the limited capacity of the ventricles to dilate during diastole, the raised venous pressure in constrictive pericarditis was without effect as a compensatory mechanism. The authors emphasized the similarity of constrictive pericarditis and congestive heart failure, characteristic features in each of these conditions being salt retention and elevation of the blood volume, and they correlated these developments with the raised venous pressure and the prolonged circulation time, each a significant manifestation in the clinical picture of the two diseases. The subjective symptomatology of constrictive pericarditis being singularly vague, it is generally agreed that its diagnosis must depend entirely on physical examination. The presenting signs may be summarized for practical purposes as those of circulatory failure without evidence of structural heart disease. Distension of the venous system is an outstanding feature in all cases. There is usually some degree of cyanosis, the neck veins are firm and engorged, the liver is enlarged, there is generally ascites, possibly also peripheral œdema, the latter located at times in the face and the upper extremities. Examination of the heart is, as a rule, singularly negative; the area of dullness and the apex impulse are usually ill-defined or entirely obscured by co-existing pleural effusion, but the size and the shape of the heart can be estimated by radioscopy and it is noteworthy that, in the majority of cases, there is little or no evidence of cardiac enlargement.

the face, the chest wall and the upper extremities, also ascites and painless non-pulsatile hepatic enlargement, all in the absence of orthopnoea.

(4) A small, low tension pulse of the paradoxical type.

Certain additional physical signs have been put forward, viz. immobility of the apex impulse, a fixed area of cardiac dullness, also systolic retraction of the apex region and the left lower intercostal spaces posteriorly; the practical value of these signs in the diagnosis of adhesive pericarditis has, however, been materially discounted by reason of the fact that they may feature other cardiac affections, notably those with considerable cardiac enlargement.

Radiological and kymographic studies furnish conclusive proof of pericardial adhesions and they should be regarded as essential items in the examination of all cases. Significant abnormalities include a decreased amplitude of cardiac pulsation and partial or complete fixation of the heart and the diaphragm during respiration; varying degrees of cardiac enlargement are usually present and, in evaluating this sign, due consideration must be given to co-existing disabilities, both valvular and myocardial; further valuable signs are the presence of visible adhesions from the pericardium to neighbouring structures, irregularities in the contour of the cardiovascular shadow, possibly also deformity and general narrowing of the retrocardiac mediastinum.

Recognition of tuberculosis as an ætiological indication in chronic pericarditis is nowadays firmly established and, assuming that the condition is diagnosed in its uncomplicated stage, there is a reasonably favourable chance that it will respond to suitable treatment. The incidence of the disease has been widely investigated both in this country and abroad. Suzman (1943) analysed a consecutive series of 1,893 autopsy records and found that in 6% of the 102 tuberculous cases there was evidence of pericardial involvement. Kornblum and his colleagues (1933) reported a 4% incidence of pericardial affection in fatal cases of pulmonary tuberculosis. Heimann and Binder (1940) studied 31 cases in the non-European hospital, Johannesburg; in some of their cases the pericarditis was a complication of a generalized tuberculæmia, 9 had signs of pulmonary tuberculosis and tuberculous root glands were present in every case; their conclusion was that tuberculous pericarditis in South African natives was not rare as a primary entity. In a recent communication, Ellman (1945) gives it as his considered opinion that tuberculosis reaches the pericardium (*a*) by the blood stream in miliary tuberculosis, or (*b*) by direct extension from a mediastinal focus, and he states emphatically that a primary tuberculous pericarditis may, for all practical purposes, be regarded as non-existent. The clinical picture of chronic tuberculous pericarditis is complex and variable. The presenting symptoms may be principally those of a pericardial effusion, or of adhesions in and around the sac, or of constrictive pericarditis in its full form and in all cases there is likely to be some degree of circulatory failure, possibly also varying phases of pyrexia; whenever possible, the pericardial exudate should be examined; a straw-coloured lymphocytic fluid is regarded as suspicious and the diagnosis of tuberculosis may, in some cases, be confirmed by culture or by guinea-pig inoculation. It is common knowledge, however, that the tests usually employed are not always infallible and that negative results do not necessarily exclude a tuberculous ætiology. Suzman (1943) recorded a case of tuberculous pericarditis, confirmed by autopsy in which, during life, the fluid was repeatedly sterile on culture, the Mantoux test negative and a guinea-pig test negative on two occasions.

Barrett and Cole (1944) reported a fatal case of tuberculous pericarditis, the early clinical diagnosis of which was confirmed by inoculation of a guinea-pig, the latter dying of generalized tuberculosis five months (an unusually long period) after inoculation. The patient, a man aged 22, was admitted to hospital complaining of general debility, a dull pain in the chest (præcordial region), breathlessness on exertion,

From the whole it is abundantly clear that, by pericardiectomy, the defective circulatory mechanics of constrictive pericarditis can be remedied to a considerable extent, the patient's subjective symptoms being thereby proportionately relieved.

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Mr. T. Holmes Sellors [Abstract]: The interest of the surgeon in chronic pericardial diseases centres on the phenomenon of cardiac compression, and it is not only on the treatment, but on the development of this state that attention should be given. The established picture with its ætiological factors is commonly recognized, but there is considerable uncertainty as to the progress and development from the earliest onset. We have been able to observe a dozen cases from their onset into the full syndrome of constriction, and, whereas polyserositis was evident in some of the cases, others simply showed a pericardial effusion.

An average picture can briefly be given as follows :

A child of 10 years had a febrile illness which was associated with a pericardial effusion; this was thought to be of rheumatic origin and the patient was kept at rest. The effusion reached considerable size, giving evidence of tamponade which was relieved by aspiration performed on two occasions. Four months later a right-sided pleural effusion developed, and at this time it was observed that the venous pressure was raised to a small degree, though the pericardial effusion itself had largely diminished. The right-sided effusion disappeared spontaneously in the course of six weeks, but a small collection then appeared in the left pleural cavity. This also absorbed, but by this time there was liver enlargement and ascites which, taken in conjunction with the rising venous pressure, suggested that constricting pericarditis was developing. This process over all took fifteen months and a further four months' rest was enforced before operation was undertaken.

In cases in which polyserositis was observed the effusion in the pleural cavities persisted in spite of aspiration, and the finding of tubercle bacilli in the ascitic fluid suggested that the peritoneum was involved by the diffuse tuberculous process. Two of these cases showed signs of pericardial constriction, but were obviously the subjects of diffuse and active tuberculous disease from which they died in eighteen months and two years respectively from the onset.

Almost every case showed evidence of its tuberculous origin, even though this was only finally established by pathological examination of the excised pericardium. The importance of recognizing tuberculosis as a cause of the condition lies in the fact that tuberculous scar tissue exerts a more powerful cicatricial effect than normal fibrous tissue, and that selection of the right time for operation in this type of case is a matter of great importance.

Many of the cases seen in adult life give little or no history of onset, and it is remarkable, judging from the extent of calcification, how the heart has been able to compensate for the restriction, probably over a period of years, before producing symptoms. There would appear to be a sudden bankruptcy which can be relieved as dramatically as it occurs on occasion by a very limited excision of pericardium. On the other hand, patients in middle or old age who develop the signs of constriction do not always do well. This may be due to the fact that heart failure has developed within the constricted pericardium which, if removed, is followed by the ordinary picture of congestive heart failure. It has also been suggested that the prolonged effect of the raised venous pressure on the liver produces permanent damage to this organ. However, in general, it is remarkable how ably the body is capable of withstanding prolonged pericardial constriction without clinical signs.

The heart sounds are best described as distant, they may be accompanied by soft systolic murmurs and pericardial friction sounds but their description otherwise does not call for special comment. The pulse is usually fast and of small volume, the blood-pressure is subnormal, its records being characterized frequently by paradoxical fluctuations. The above-mentioned signs should in all cases be confirmed by radiological and kymographic investigation, the value of which, in the accurate diagnosis of constrictive pericarditis, is both fundamental and impressive. The heart shadow may be normal in size or slightly enlarged owing to varying degrees of thickening of the pericardium; the heart's pulsation may be feeble or absent entirely and the outlines of its chambers are in varying degree obscured; the heart and the mediastinum may be fixed and displaced, the retrosternal and the retrocardiac spaces obliterated; the margins of the pericardium may be irregular and the presence of calcified plaques is frequently noted; there may be visible adhesions from the pericardium to the neighbouring viscera and, if these are attached to the diaphragm, its puckered surface and its limited range of excursion are clearly defined. The cardiogram may provide valuable supporting evidence in the diagnosis of constrictive pericarditis; characteristic discrepancies of the curves include low-voltage complexes and flattening or inversion of the T waves in the præcordial as well as in the limb leads; Graybiel and White (1946) have suggested that these appearances, which closely simulate coronary heart disease, are due to sub-epicardial myocardial inflammation and scarring; not infrequently there are changes in the R-T segments and in the T waves similar to those recorded in acute myocardial infarction but, as Ellman (1945) has noted, the Q waves are not exaggerated in constrictive pericarditis and the direction of the R-T segments and the T waves are similar in all the leads.

In common with the increasing number of cardiovascular diseases which are being subjected to operation, the treatment of constrictive pericarditis exemplifies in ample form the existence of an intimate liaison between physicians and their surgical colleagues. Pericardiectomy is nowadays firmly established as the approved remedy for patients suffering from constrictive pericarditis who are otherwise in a sufficiently favourable condition to undergo a major operation. Circulatory measurements are essential in the selection of cases and their comparative estimates before and after operation are of considerable prognostic importance. The measurements include readings of the venous blood-pressure, the total blood volume, the cardiac output per minute, the cardiac output per beat, the vital capacity, the circulation time and the arterial blood-pressure (*see* Table I). Lyons and Burwell (1946) reported 2 cases of constrictive pericarditis including with each a series of circulatory measurements made under standard conditions both before and after operation and the following is a typical extract of their findings on one case:

TABLE I

	Normal values	Case I before operation	Case I after operation
Venous blood-pressure mm. water	Below 150	217	108
Total blood volume in c.c.	5,400	6,570	5,300
Heart rate per minute	64	74	70
Oxygen consumption per minute	231	213	196
A-V difference vol. O ₂ per litre blood ..	59.0	65.0	51.5
Cardiac output in litres per minute ..	3.87	3.28	3.83
Systolic output in c.c. per stroke	60.4	44.0	53.2
Blood flow in litres per sq. m. surface area ..	2.21	1.89	2.06
Vital capacity in c.c.	4,350	2,500	2,500
Circulation time in seconds	15-20	41	34
Arterial blood-pressure mm.Hg	120/80	114/74	110/70

The more significant features of Table I are the post-operative lowering of the venous blood-pressure with an increased cardiac output and blood flow, a diminished blood volume and an increased circulation rate.

lateral approach avoids the difficulty of a low-placed or big breast in women and is satisfactory for secondary operations, when only slight or moderate improvement has been obtained after an anterior excision.

The exposed heart, once the lung has retracted, is covered with loose fibro-fatty tissue which is vascular. When this is removed the yellow-white casing of the pericardium is seen and an incision is made into this on a site which avoids the anterior branch of the left coronary artery. It is often difficult to establish the right layer for a start and judicious dissection must follow until the brown (and bloody) muscle fibres are exposed. Once flaps have been raised the dissection is continued, either as far as the limits of the ventricular exposure will allow, or as far as the general condition of the patient permits. Extrasystoles are common during manipulation and the heart should be given regular periods of rest to prevent gross arrhythmia. Superficial bleeding from muscle usually stops spontaneously, but, if persistent, fibrin foam or muscle patches may be required. Tearing of heart muscle is an obvious danger and is most likely to occur near the auriculo-ventricular groove, or over the thin-walled right ventricle. The pericardial flaps should not be cut away until the dissection is complete since in emergency they could be sutured over a tear in the muscle. No ligatures must be applied to the coronary vessels.

The results in 21 operation cases are fairly satisfactory. Three deaths occurred, one some hours after operation probably from ventricular fibrillation, the other two died before operation was started following a very small dose of pentothal. In both cases the chest was opened with the minimum of delay and though in one case the heart was started again the patient died without recovering consciousness. In the other instance no response at all could be elicited from the heart muscle in spite of various stimuli applied to it. The remaining patients recovered from the operation with one exception who died of congestive heart failure some time later. Out of the 17 survivors 14 are performing some form of work or have normal activity, though critically some of these would not pass as completely fit. It has been noted that reduction in the venous pressure, after an initial good post-operative fall, is slow and four to six months should be allowed to elapse before deciding on the final figure. The same applies to enlargement of the liver, but ascites subsides rapidly and we have not had to remove abdominal fluid in any case after operation.

Diagnostic errors can occur and on two occasions we have explored the pericardium for suspected constriction to find, in one instance, a gross tricuspid lesion and in the other thrombosis of the right auricle and venæ cavæ. These cases may be quoted as illustrating some difficulties in diagnosis, since the clinical picture was identical with many of the constrictive lesions on which we operated.

In the hands of an experienced thoracic team the risks of exploration of the pericardium are small and it is felt that if all other means have failed to establish diagnosis operation should be considered. In our own experience this course was justified in a number of cases where definite constriction was recognized without the classical signs and symptoms being present.

Dr. Peter Kerley: Radiological examination of pericardial diseases, other than large effusions, has been greatly stimulated by the successful surgical treatment of adhesions which interfere with normal cardiac function. Scarcely a month passes without some new report of such cases in one of the many radiological journals and as a result we are overburdened with descriptive signs many of which are unreliable or applicable only to a particular case. Assessment of the value of these signs and of the various techniques required to demonstrate them is no easy task. Every radiologist viewing large numbers of chest cases often sees cases of gross chronic pulmonary disease with obvious pleuro-pericardial adhesions and even kinking or torsion of the great veins without any clinical evidence of cardiac embarrassment. Conversely we

The selection of time for the operation is largely influenced by the probability of the tuberculous origin, and, as has been said, in children the maximum period of bed rest must be allowed to enhance quiescence of disease process. In adults or elderly people quiescence may be assumed and only a short period of preparation and assessment be required.

In a series of 45 cases which we have observed tuberculosis has been established in the majority. Untreated suppurative pericarditis was a probable cause in one instance, and there were 4 cases of undetermined origin. Rheumatic pericarditis did not produce constriction, though, on occasions, it produced transitory cardiac tamponade.

The classical description of the heart in this condition is not always accurate, for though this organ may appear small and quiet, it is always possible to have a large heart outline which sometimes shows quite obvious pulsations. The enlargement of the heart may be due to the actual thickening of the pericardium and movement may be more obvious in some parts of the heart than in others.

Treatment.—A pericardial effusion may require aspiration for diagnostic purposes as well as for relief of pressure. This procedure may have to be repeated and gas replacement is sometimes of value in demonstrating the thickness of the parietal pericardium, as well as the size of the heart itself. The site for aspiration should be made from below between the costal margin and xiphisternum, puncturing through the diaphragm the lower part of the pericardial sac. The risks of pleural damage and hæmorrhage when the anterior intercostal routes are used should lead to their exclusion. On two occasions I have performed a deliberate excision of the left parietal pericardium to allow a persistently accumulating effusion to drain into the larger surface of the pleural cavity, and then at a later date proceeded with excision of the organized visceral layer.

The treatment of established constriction is excision of both layers of the pericardium. A preliminary period of rest accompanied by efforts to reduce ascites or other effusions is indicated. Mercurial diuretics with a restricted fluid intake help to improve the general condition.

The planning of pericardial excision is based on the fact that the essential mechanical problem lies in the prevention of the full diastolic phase of the ventricles. This was originally fully described by Richard Lower and is certainly more acceptable than the assumption that a constriction occurs round the caval orifices and auricles. Constriction can certainly occur over these areas, but it is not of great importance and can hardly be remedied with safety by surgery. Both ventricles should be freed as far as circumstances permit, with the proviso that the right heart must not be freed too extensively before the left to prevent possible pulmonary congestion. The general condition of the patient may not allow full excision and then every endeavour should be made to free the apex and left border of the heart. Both layers of the pericardium, as has been said, must be excised so that the actual heart muscle itself is exposed. Anæsthesia is most satisfactory with controlled endotracheal ether and oxygen. Cyclopropane allows an agreeably high concentration of oxygen, but leads to cardiac irregularities. Barbiturates are best avoided, as also chloroform.

The original standard exposure of the pericardium was designed as an extrapleural operation, but the difficulty of access to the left border of the heart without tearing the pleura was considerable. The present view is that the approach to the heart should be through a deliberate transpleural incision, which can be (1) through the third left interspace with division of one or more costal cartilages, or (2) posteriorly following excision of the seventh or eighth rib. Anteriorly the heart is closer to the surface and the mediastinum is stable, but there is less room, while the posterior approach finds the heart at a deeper level and may be a difficult exposure if there has been pre-existing pleurisy. I prefer the anterior incision especially with bad risks where only a small preliminary pericardiectomy may be permissible. The postero-

Since there are not many kymographs about, I will deal with the major radiological signs on the basis of investigation by any reasonable standard equipment. First and foremost is alteration in the shape of the heart. It is very unlikely that any adhesions of consequence can be present without altering the shape in one plane or another. Since the site most affected is the right border and the anterior surface we should concentrate on these—moreover these are two aspects where we are less likely to be misled by co-existing mitral or aortic disease. A continuous convex right border from



FIG. 1.—Obliteration of the normal cardiac contours on the right side. This heart was adherent to the sternum.

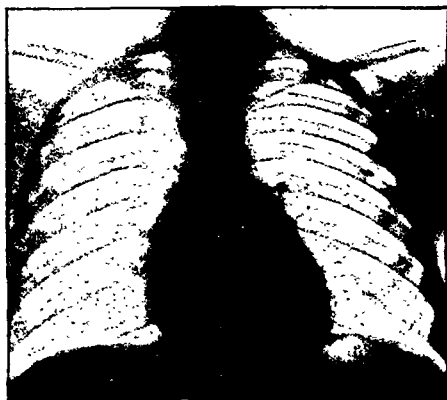


FIG. 2.—Obliteration of the normal contours on both borders of the heart. The small pear-shaped heart is typical of extensive intrinsic adhesions.



FIG. 3.—Dense extrinsic and intrinsic pericardial adhesions with pleural obliteration at both bases. The heart has a triangular shape.

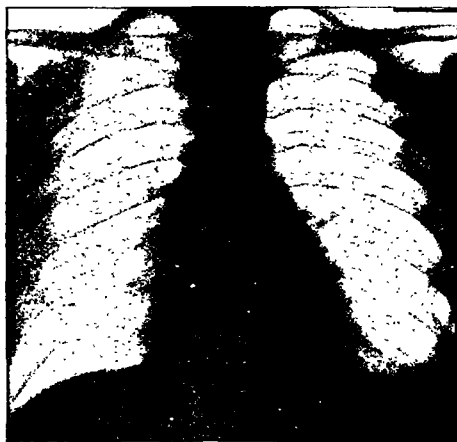


FIG. 4.—Extrinsic and intrinsic adhesions. The right border is straight and the left border round. On both sides the normal contours are obliterated.

diaphragm to aorta is the most consistent alteration in shape in constrictive pericarditis, and a dilated vena cava above this is strong corroborative evidence. A similar continuous convex curve is seen on the left border in the presence of extensive intrinsic adhesions. The heart then is globular or pear-shaped like a pendant (fig. 2). Less frequently the borders are quite straight and the heart has a triangular or polygonal shape (fig. 3). Combinations occur with one border straight and one convex (fig. 4).

occasionally stumble on cases with obvious deforming pericardial adhesions or even pericardial calcification where symptoms have been dismissed as functional or wrongly attributed to associated valvular or myocardial disease.

The radiological findings in a gross case are irregularity of the cardiac borders, diminished or absent pulsation, limited diaphragmatic movements and associated pleural thickening. In advanced cases it is comparatively easy to deduce from the shaggy radiological mass that pericardial adhesions are present but in cases of minor degree in which the adhesions may be no less disabling, there are many variations of these signs. Accurate analysis of them with the most exacting technique is necessary if we are to get anywhere near a precise anatomical diagnosis.

A simple screen examination and a few straight pictures may be sufficient to demonstrate fixation of the heart but it is certain that many of what I will call the sub-clinical cases will be overlooked if we rely on these standard procedures. The patient must be examined in both supine and erect positions and, above all, it is necessary to take the lateral pictures in the recumbent position. In at least one frontal and one lateral view a grid should be used and that much underrated instrument, the X-ray kymograph, can, despite its defects, sometimes prove diagnostic.

Usually we are dealing with combinations of extrinsic and intrinsic adhesions, the former offering resistance to systole and the latter preventing the normal systolic-diastolic change in form and position. Surprising combinations of both occur and of course the whole radiological picture may be complicated by associated valvular disease.

The radiologist's job is first to prove the presence of adhesions and secondly to locate them accurately. If he can do this his evidence may determine the necessity or otherwise for surgical interference and even indicate the most suitable surgical approach.

We know from both living records and autopsy experiments of fluid in the pericardium that the most dependent part of the pericardial sac is that area around the apex and on the posterior border of the left ventricle. This is also the area of greatest movement. As an effusion is absorbing the residual fluid gravitates into this corner and the vigorous left-sided thrust of the heart tends to squeeze residual fluid out over the relatively quiet right border and sternal aspect of the right ventricle. The majority of adhesions are right-sided and anterior, and although they may be very disabling they can cause little apparent distortion of the shape, size, position and pulsation of the heart. The following case is a classical example of this type of adhesions:

The subject is a doctor who in 1929 had pneumonia and pericarditis was also suspected. On recovery from the acute stage he had dyspnoea which was attributed to myocardial damage on the basis of abnormal electrocardiographic findings. He had an inverted T wave in leads 1, 2 and 3. Subsequently 1 and 2 reverted to normal. Some years later when in America he again had dyspnoea and after a very full investigation by an eminent cardiologist was told he had a coronary thrombosis. He came to England and before joining the Army consulted another cardiologist because of excessive pulsation in the veins of his neck. He was assured that this was anatomical and that he had a cardiac neurosis. He served overseas, and again complaining of dyspnoea after several attacks of malaria, was correctly diagnosed as adhesive pericarditis by Dr. Evan Bedford. It was left to his wife, however, to detect his calcification on what I think was an indifferent X-ray picture. The straight picture (fig. 1) shows a normal-sized heart but two obvious abnormalities—a convex right border from diaphragm to aorta without an intervening notch at the level of the lung root, and a distended superior vena cava. On an over-penetrated picture a ragged area of calcification was visible but easily mistaken for disease in the lung. In the first oblique view there was apparent enlargement of the heart to the left but no calcification was visible. The second oblique view showed a small heart again without visible calcification until a grid and a kymograph were used. The kymographic pictures taken at the same distance clearly show the whole pathology. His heart is firmly adherent to the sternum, partly adherent to the base and probably completely stuck on the right border up to the exit of the superior vena cava (figs. 5, 6 and 7). The P.A. kymograph shows another useful sign—increased pulsation on the left border with a relative decrease of pulsation on the aorta (fig. 5). The reason for this is discussed later.

emphasis is laid on the small quiet heart for it tends to make us forget that disabling adhesions also occur with normal and large hearts. The possibility of adhesions forming in an already enlarged heart should always be kept in mind. In such a case the adhesions may be responsible for hepatic enlargement and ascites, and the differential diagnosis from right-sided congestive failure can be made by the radiological demonstration of a small right ventricle and auricle. Schwedel gives a beautiful demonstration of this. A chronic encysted effusion may also cause enlargement of the heart shadow but of an eccentric type and Roesler describes enlargement due to a pericardium over an inch thick.

It is uncommon to see the heart markedly displaced to one or other side. Adhesions at the base keep it in a central position even when there are gross pleuro-pulmonary adhesions and fibrosis which one would expect to cause a lateral drag. Basal adhesions prevent the heart from moving upwards during inspiration but this sign is also present in a big heart without any adhesions. If the diaphragm is free except under the base of the heart, the medial and tendinous portions will be stationary during inspiration while the lateral parts will move steeply downwards. This causes apparent elevation of the heart during inspiration—an optical illusion similar to the sensation of movement in a stationary train when another on the neighbouring track moves forward slowly.

If the anterior surface of the heart is adherent to the sternum the retrosternal space is opaque and does not widen or illuminate during deep inspiration. Occasionally one can directly visualize bands between the heart and the sternum. Similar phenomena can be demonstrated in the posterior mediastinum with posterior adhesions. Unless, however, one can actually see bands of adhesions reduction in size and illumination of these spaces is an unreliable sign for there are too many normal variations. If the heart is enlarged these signs are valueless.

Much valuable information can be gained by studying the movement in the lateral recumbent position and this should be done on both sides. In this position the normal heart sags to the dependent side during expiration and moves away from it on inspiration. Absence of this inspiratory shift is proof of extensive external adhesions. This sign only becomes invalid if there is a big heart with congestive failure and fluid in the pericardial or pleural cavities.

Abnormalities of pulsation are frequent and although best observed on a kymograph the major ones can be detected by screening. Pulsation is increased or decreased according to the underlying pathology. With severe constriction pulsation is absent or negligible. If one area is free it shows increased pulsation. If this free area happens to be the left border, the increased pulsations are in marked contrast to diminished pulsations on the aorta (fig. 5). The increased amplitude on the ventricular border does not represent an increased stroke volume but is merely an increased marginal excursion to compensate for loss of movement.

If we find absent or very feeble pulsation without evidence of circulatory embarrassment we can infer that the adhesions are linear and that the pericardial sac is not obliterated. Roesler believes that absent pulsation with a normal circulation is proof of the persistence of movements of the atrio-ventricular septum.

In most cases the pulmonary vessels are normal or show only slight congestion, a striking anomaly if there is congestive failure in the greater circulation. The absence of pulmonary stasis is explained by the fact that the disease usually affects the right heart more than the left. It is a curious fact that even big pericardial effusions seldom compress the left auricle and nearly all writers on calcification of the pericardium comment on the rarity of calcification in the region of the left auricle.

Calcification of the pericardium is of course the radiological hall-mark. We do not know in what percentage of cases it occurs but it is certainly not seen very often. The calcified deposits may be granular, linear or coralliform and combinations of all

An absolutely straight border indicates involvement of the mediastinal pleura and external fixation. In the pear-shaped heart the cardiophrenic angles are free while in the triangular-shaped heart these angles are usually obliterated but care should be



FIG. 5.—Kymograph of an unsuspected case of adhesive pericarditis. This heart is adherent anteriorly and on the right. The left border is free. Note the abnormal increased amplitude on the left ventricular border as compared with the normal amplitude on the aorta. Same case as fig. 1.



FIG. 6.—Same case in the first oblique view. There is apparent enlargement of the heart to the left.



FIG. 7.—Same case in the second oblique view. The heart is apparently small and a ring of calcification to the sternum and base is clearly visible.

taken not to confuse normal fat deposits with such obliteration. The superior vena cava is often wider and denser than normal and the aortic knuckle is small. If the mediastinal pleura on the left side is extensively involved the aortic knuckle may be invisible or its convex outer border may appear straight. Localization of adhesions to certain areas may cause free areas to bulge like a hernia. If the apex escapes it may bulge like a cardiac aneurysm while if the posterior border escapes it may bulge like an enlarged left auricle. Extensive adhesions, either extrinsic or intrinsic, usually obliterate all radiological signs of associated mitral or aortic disease.

As a rule the heart is central in position and small. In some ways too much

Section of Laryngology

President—A. J. WRIGHT

[March 5, 1948]

DISCUSSION ON MALIGNANT DISEASE OF THE PHARYNX, EXCLUDING THE NASOPHARYNX

J. F. Simpson: *Cancer in the laryngopharynx.*—The gravity of this problem is shown in the report for 1945 of the Clinical Research Committee of the British Empire Cancer Campaign which states that out of 384 cases of laryngopharyngeal cancer only 19 survived the five-year period. Similarly in 1946 the Holt Radium Institute, Manchester, reported that out of 220 cases 9 cases survived the five-year period. It is because the symptoms are insidious that presentation is often late and to many palliation is all that can be offered. The early symptoms may be no more than a mild pricking sensation in the throat and slight muffling of the voice or a "catch in the swallow". An enlarged gland may be the first manifestation in pyriform fossa growths in as many as 25% of the cases. This symptomatology is in marked contrast to that of cancer of the vocal cords and is reflected in the expectation of cure.

When choosing between surgery and irradiation as the method of treatment it is sometimes difficult to suppress a personal bias, but it is essential that each case should be considered individually and not as a member of a group. The histology of the neoplasm and its operability are decisive factors in the choice of treatment. When the tumour is found to be of a type known to be especially amenable to radiotherapy the choice must be irradiation. Such tumours will include lymphosarcoma, reticulosarcoma, lympho-epithelioma and basal-cell carcinoma. These are more common in the nasopharynx and oropharynx but when occurring in the laryngopharynx generally originate in the vallecular region. These tumours spread early to the glands and the entire lymphatic field must always be treated at the same time as the primary focus.

Secondary growths are occasionally encountered in the laryngopharynx and require irradiation. The following three examples were recently encountered: an oat-celled bronchial carcinoma in the pyriform fossa which presented as the first evidence of malignant disease; a papillary carcinoma of the thyroid invading the posterior wall in a man of 21 in whom the primary growth had apparently been successfully removed a year previously; and thirdly, an example of a multicentric growth showing as scattered nodules. This was seen six months after the removal of a minute carcinoma from the floor of the mouth.

The vast majority of tumours in the laryngopharynx are squamous-cell carcinomata and laboratory aids have not as yet superseded the clinical assessment in the decision as to choice of treatment. The grading of squamous-cell carcinoma as described by Broders may indicate the liability to metastasize but it appears to carry little weight to-day in the prediction of the response of the individual tumour to irradiation. Even serial biopsy under irradiation is not without its errors. Constant clinical observation during and after treatment seems to be the only means of judging its effect. This is a matter of the utmost importance and should be carried out by the radiotherapist and the surgeon consulting together.

Inoperability is an indication for irradiation of carcinoma but this is a relative term as "inoperable cases in some hands become operable". Apart from the general physical condition and temperament of the patient the glandular metastases usually determine operability.

Current opinion seems fairly agreed upon the lines of treatment in regard to the glandular metastases. A search for glands should always be made during the excision of the primary growth, even though none was detected on clinical examination. Where none is found and the excision is considered satisfactory, it is better to place reliance on post-operative observation than to embark upon immediate routine post-operative irradiation.

If the primary focus has been successfully treated by external irradiation through the gland fields but with failure to control the glands themselves these should be removed surgically if possible. The temptation to give a second course of therapy whilst they are still operable must be resisted. Thus whenever possible glandular metastases must be excised where the primary focus has been successfully treated, whether by surgery or irradiation.

Operations on the laryngopharynx are now largely standardized and during the last few years operative mortality has decreased with the introduction of chemotherapy and the antibiotics together with improved methods of anaesthesia. Other aids, such as con-

three may be found together. The sites of preference for calcification are the coronary sulcus, the diaphragmatic surface and the sternal aspect of the right ventricular area. The left ventricular area with the exception of the apex comes next. Rarely do we find the whole sac armour-plated. Pericardial calcification must be differentiated from a calcified infarct and intracardiac calcifications. An infarct in the common site on the left border is easy to diagnose by the shelf-like projection in the first oblique view but an apical infarct might be very troublesome. Calcified valves and calcified thrombi show considerable and characteristic movements. A calcified left auricle may look very like pericardial calcification but it usually forms a complete ring, can be localized to the left auricle and on the kymograph shows auricular pulsations. There is no X-ray evidence which throws any light on the ætiology of the uncalcified types unless there is associated pulmonary tuberculosis. Some years before the war we had a case in Westminster Hospital in which the causative agent was actinomycosis but the visible lung changes of pulmonary suppuration might have been produced by any of the common organisms. Occasionally we see pericardial effusions secondary to carcinoma of the lung but I have not known one live long enough to be deemed chronic. (I have a strong suspicion that deep X-ray therapy may cause adhesive pericarditis and that not all the superior vena caval obstructions are due to malignancy. Deep therapy can certainly produce pleural obliteration.)

Looking through the literature on calcification of the pericardium, one finds opinion about equally divided on rheumatism and tuberculosis as the cause. If we postulate a similar basis for pleural and pericardial calcification, blood would be a most important factor. The large-scale mass radiography surveys have shown 10 cases of pleural calcification following trauma for every one due to tuberculosis. There are a few reports of pericardial calcification following trauma. Glenn describes its development two years after a crush injury, Schwarz has one case following a heavy direct blow over the heart and Zdansky one as a sequel to a stab wound.

We have not yet exhausted all the possibilities of radiological investigation of the pericardium. It is certain that we will have first-class X-ray cinematography in the next year or two. I made a brief mention of tomography earlier on. Looking over some tomograms I was struck by a number in which a double shadow of systole and diastole was quite sharp and clear. It is only a question of selecting the right penetration and accurately timing the tomographic movement with the heart rate to reproduce this in any given case and there are no insuperable mechanical difficulties. There are certainly possibilities in the method; it would be much cheaper than either kymography or cinematography and capable of adaptation to any standard equipment.

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tinuous suction drainage and the use of semidigested protein foods to give a high concentration with tube feeding, may play a part.

The surgery may be divided into two types: (1) Simple excision without serious loss of structure or function, i.e. lateral transthyroid pharyngotomy; (2) large mutilating operations in which structures are sacrificed, i.e. pharyngolaryngectomy.

There is an intermediate group in which plastic procedures are necessary to make good the excised portion of the pharynx and to restore function:

When the neoplasm has invaded the framework of the larynx so that its removal is required, as much of the pharyngeal mucosa as possible is left so as to join the oropharynx with the œsophagus, but the entire segment of pharynx may have to be removed with the larynx. Recent American publications have stressed the necessity of removing the hyoid bone and tongue tissue above it in some cases to reduce the chance of recurrence in the pre-epiglottic space—a point too often disregarded here.

Because of the advanced state of the disease and poor condition of the patient when first seen irradiation and not radical surgery is the treatment more frequently applied. Furthermore, irradiation can be applied to almost every case, but this must not be taken to mean that irradiation is the only form of treatment for cancer of the laryngopharynx, a belief too prevalent to-day. Radiotherapists recognize that the response to irradiation varies at the different sites in the laryngopharynx and comparatively good response is expected in the vallecula, epiglottis and aryepiglottic fold but the black spots of the laryngopharynx are the pharyngeal wall, pyriform fossa and the post-cricoid region.

This clinical fact must always be taken into consideration when planning treatment and will naturally give bias towards irradiation in the favourable sites. It is in these same places with the exception of the vallecula that the more limited form of surgery may be applicable when the growth is small. The choice between such surgery and irradiation as a first line of treatment in these cases is a difficult one. Every aspect of each case must be weighed, the selection being highly individual and set rules cannot be applied. It is in these positions that a carefully watched therapeutic trial of irradiation may yield good results, especially when the growth is superficial and non-infiltrating. If a full course fails to produce complete disappearance of the cancer a second course will not produce a cure. It follows, therefore, that as soon as irradiation is thought not to be controlling the disease urgent consideration must be given to the possibility of radical surgery. This revision of treatment may supply the last and only chance of prolonging life, apart from a possible cure.

The formidable nature of the operation of median translaryngeal pharyngotomy together with the fair expectation from irradiation rules out surgery for vallecular growths. It is rare for pyriform fossa and post-cricoid carcinomata to be suitable for local excision but when such surgery is possible it should be given every consideration on account of the unfavourable response to irradiation at these sites.

Once any carcinoma of the laryngopharynx is thought to have invaded the cartilage of the larynx, with the exception of the free portions of the epiglottis, it is best to give first place to surgery even though this means pharyngolaryngectomy. All these decisions are of course made in the light of the state of the lymphatic glands, &c. They should not be made by the surgeon or radiotherapist working alone but as a team in which consultation results in planned attack. Furthermore, observation after operation or radiotherapy forms one of the most important responsibilities which this team must undertake.

Statistics have been avoided as almost every individual case must in the end require a separate category and this makes comparison dangerous, but some figures must be quoted to appreciate the degree of success which may be obtained by surgery. Lionel Colledge was able to state in his Lettsomian Lecture, Medical Society of London, 1943, that 13 out of 39 patients (33%) were well ten years after lateral pharyngotomy and 6 out of 16 cases (37%) for a similar period after pharyngolaryngectomy. These figures undoubtedly represent the peak to which this branch of surgery has been brought. Last year Orton of Newark presented to the American Laryngological Association a series of 51 cases of pharyngeal carcinoma in which surgery was the method of treatment and resulted in 27% of five-year cures.

In the British Empire Cancer Campaign already referred to there were 49 cases in which there were no glandular metastases or invasion of the adjacent tissues. Of these only 2 were subjected to radical surgery (pharyngotomy). The two cases which received surgery survived the five-year period and 6 out of the 47 which received irradiation (13%).

The treatment of cancer of the laryngopharynx must be carried out by a team. The possibility of good surgical results in suitable cases must be remembered in view of the Cancer Act. If this Act means that patients are to be sent direct to the radiotherapist without the benefit of surgical opinion it will be a sad thing, but if it means consultation and following up by a team then we may reasonably expect improvement in results in the integrated use of the only two weapons at our disposal.

R. S. Pilcher: In 100 consecutive cases of cancer of the pharynx admitted to University College Hospital there were 70 men and 30 women. Men had a maximum incidence at 60-64, women at 50-54. In 29 women the growth was post-cricoid, in 1 woman and 70 men the growth was epilyngeal. In the epilyngeal group two sites are important, the pyriform fossa because of its frequency (42 cases), the lateral wall because it is the most favourable for conservative surgery (9 cases). Observations on the symptoms show further distinctions between the epilyngeal and post-cricoid groups. Dysphagia was the first symptom in 11 women, but only 10 men. It was, however, the dominant symptom on admission in 25 women and 32 men, the average duration of symptoms before admission being eight months. Enlargement of cervical glands was the first symptom in 22 men, but only 1 woman. While it is true that the post-cricoid growth is less likely to be symptomless than one in the pyriform fossa and, therefore, more likely to be noticed before it has metastasized to glands, it also appears that the former metastasizes less rapidly than the latter. Even a large post-cricoid cancer with over a year's duration may remain localized to the primary site. The distinction is important for in the epilyngeal group it is often the glandular metastases that determine inoperability, while in the post-cricoid it is usually the local spread of the primary. Gland dissection should always form part of the surgical treatment of the epilyngeal growth, but may sometimes be omitted in the post-cricoid. Common to the symptoms of both groups is the onset with some abnormal but trivial sensation in the throat. These sensations, which are variously described by the patients, were the first symptoms of the disease in 30 men and 13 women. Suggestive of cancer, when a patient complains of an abnormal sensation in the throat, is its definite localization and its persistence. Indirect laryngoscopy for any persistent localized discomfort in the throat is the most promising contribution to early diagnosis of cancer of the pharynx.

Of the 100 cases, 49 were judged to be operable—35 men and 14 women. Estimates of operability vary widely, but that this series is not a particularly favourable one is suggested by the need for emergency tracheotomy or gastrostomy, or both in 25 cases, apart from the use of these measures as part of radical treatment. Radical operations were completed in 25 men and 14 women with 9 operative deaths in the former and 7 in the latter. 4 men and 3 women survived five years or more without recurrence, the shortest observed period being five years, the longest 14 years. All operations were of the conservative type and the series includes no example of pharyngolaryngectomy. The chief cause of mortality was sepsis and none of the operations in the series was performed later than 1935 when the benefits of chemotherapy were not available. In addition to the cases treated surgically there were two survivals of five years or more after irradiation—both being operable cases. One of these had repeated local recurrences before five years and died of the disease. The total of five-year survivors out of the 100 cases was, therefore, 9 and of these 8 survived five years or more without recurrence.

The aim of the conservative operation devised by Wilfred Trotter is to remove the growth and to preserve the functions of the larynx and pharynx. It is sometimes possible, particularly if the growth is on the lateral wall, to reconstitute the pharynx by simple suture of the defect, but usually a 2-stage operation with replacement by skin is necessary and incisions are planned with this in view.

For post-cricoid tumours excision of the whole circumference of the pharynx is usually necessary and to replace this the incision outlines a rectangular flap, with its free end in front, which will, at the second stage, be rolled into a tube. From the base of the flap the incision is continued up to the mastoid and down to the clavicle.

For the epilyngeal tumours smaller areas of skin replacement are needed and flaps hinged on the mucocutaneous junction made at the first stage are adequate. The skin that is turned in at the second stage to form new pharyngeal wall should be taken from below the lower edge of the beard. The main skin incision for epilyngeal growth should be a curved one across the neck just below the beard line. From the centre of this another incision can be made down to the clavicle. When the pharynx is closed no skin for turning in should be taken from above the transverse incision. After the skin incisions have been made according to the expected plan of reconstruction and flaps raised the next step is the gland dissection. The sternomastoid is usually retained and is sutured to the prevertebral fascia in front of the carotid sheath to afford the latter some protection from infection. To expose the pharynx, one-half of the thyroid cartilage is removed and sometimes half the hyoid bone. If the growth involves the thyroid the ala is not completely removed, but is left attached after division of the cartilage in the mid-line. The pharynx is opened at any convenient point at least a centimetre from the edge of the tumour as determined by palpation, and from this opening excision is completed with the pharyngeal aspect of the growth in view. If a post-cricoid growth encircles the pharynx separate openings must be made above and below. After excision of the growth mucosa is sutured to skin all round the defect, making a single stoma for an epilyngeal growth and usually a double one for a post-

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Once any carcinoma of the laryngopharynx is thought to have invaded the cartilage of the larynx, with the exception of the free portions of the epiglottis, it is best to give first place to surgery even though this means pharyngolaryngectomy. All these decisions are of course made in the light of the state of the lymphatic glands, &c. They should not be made by the surgeon or radiotherapist working alone but as a team in which consultation results in planned attack. Furthermore, observation after operation or radiotherapy forms one of the most important responsibilities which this team must undertake.

Statistics have been avoided as almost every individual case must in the end require a separate category and this makes comparison dangerous, but some figures must be quoted to appreciate the degree of success which may be obtained by surgery. Lionel Collidge was able to state in his Lettsomian Lecture, Medical Society of London, 1943, that 13 out of 39 patients (33%) were well ten years after lateral pharyngotomy and 6 out of 16 cases (37%) for a similar period after pharyngolaryngectomy. These figures undoubtedly represent the peak to which this branch of surgery has been brought. Last year Orton of Newark presented to the American Laryngological Association a series of 51 cases of pharyngeal carcinoma in which surgery was the method of treatment and resulted in 27% of five-year cures.

In the British Empire Cancer Campaign already referred to there were 49 cases in which there were no glandular metastases or invasion of the adjacent tissues. Of these only 2 were subjected to radical surgery (pharyngotomy). The two cases which received surgery survived the five-year period and 6 out of the 47 which received irradiation (13%).

The treatment of cancer of the laryngopharynx must be carried out by a team. The possibility of good surgical results in suitable cases must be remembered in view of the Cancer Act. If this Act means that patients are to be sent direct to the radiotherapist without the benefit of surgical opinion it will be a sad thing, but if it means consultation and following up by a team then we may reasonably expect improvement in results in the integrated use of the only two weapons at our disposal.

carcinoma of the tonsil which have extended a few millimetres into the base of the tongue. The response of the growth in the tonsillar fossa has been most successful, but the response, with identical dosage, of that portion of the growth invading the tongue has been poor, and active growth has persisted there. This difference in response can only have been due to the difference in the tumour bed.

With reference to tumours of lymphatic origin. Although there are not a large number of them it is important that they should be recognized as their treatment and prognosis are different from that of the squamous carcinomata.

Any of the members of the group of lymphomata, such as lymphosarcomata, reticulum-cell sarcomata, may give rise to tumours in the oropharynx. They may cause diffuse enlargement of the tonsil similar to ordinary tonsillar hypertrophy. The tumour projects from the tonsillar fossa as a rounded or irregular-shaped mass which may attain a considerable size.

At first the tumour does not appear to infiltrate the surrounding tissues. As the tumour progresses, it infiltrates the pillar and encroaches diffusely upon the soft palate. It may also extend into the base of the tongue. There may be superficial ulceration. The consistency of the tumour is harder than normal tonsil, but usually it is softer than carcinoma. The metastases in the cervical glands are comparatively soft and isolated in the beginning. They become fixed to surrounding tissues at a fairly early stage, but they are rarely adherent to the skin.

A lymphoma in the pharynx is only one manifestation of a generalized disease. The disease may remain localized in the throat for some months, or even many years, but sooner or later enlarged glands will appear elsewhere in the body, such as enlarged axillary or inguinal glands, or enlarged mediastinal or abdominal glands; or deposits may arise in the liver, spleen or bones. It is important to realize the widespread tendency of this growth from the very first. A complete examination of the patient should therefore be made. So often one is asked to treat a patient with a tumour in the pharynx and on examination one finds enlarged glands elsewhere in the body. Naturally it is useless to treat the tumour in the throat only.

(A table of the age-incidence in the 89 cases was shown.)

Most of the patients were between 50 and 80 years of age. There were relatively few under 50. There were more males than females. 10 of the 20 women had post-cricoid carcinoma.

In deciding between operation or radiotherapy, all patients were seen by both the surgeon and the radiotherapist, and the various methods of treatment discussed.

Cases of cancer of the pharynx with an operable tumour can be treated and cured by the operation of lateral pharyngotomy or pharyngolaryngectomy. The majority of cases, however, referred to the radiotherapist are already inoperable; or if they have an operable tumour, their general condition is too poor to stand a big operation. During the last three years, any operable cancer of the hypopharynx, including the post-cricoid cancers, was operated on if the patient was in a fit condition to stand an operation. The number of cases treated by surgery alone show how few were considered suitable for operation.

Inoperable cancers of the hypopharynx were treated by radiotherapy. Squamous carcinomata of the oropharynx were treated in one of two ways. In a few cases part or the whole of the tumour was removed by diathermy and then X-ray treatment was given, and in the other cases irradiation alone was used. All tumours belonging to the malignant lymphomata group were treated by radiotherapy alone. We do not consider that they are suitable for surgery, since they are only one manifestation of a generalized disease, and we consider there is a risk of general dissemination of the growth if the tissues are cut into. These tumours are all radiosensitive.

Great care was taken in planning the technique of irradiation treatment, especially in estimating the extent of the growth. It is of utmost importance to know the limits of the growth, otherwise the area of irradiated tissue may be inadequate and parts of the growth may be untreated.

Œsophagoscopy and direct laryngoscopy are usually necessary to determine the full extent of the growth, and even then it may be impossible to pass the œsophagoscope beyond the growth and find the lower end. A lateral straight X-ray of the soft tissues of the neck either with or without barium in the pharynx or cervical œsophagus, and also tomographs may be of immense help, particularly in post-cricoid cancers.

One of the chief hindrances to the successful treatment of cancer of the pharynx is sepsis. Sepsis not only renders the growth more radioresistant, but makes the patient more likely to succumb to some infection of the lungs, such as bronchopneumonia. It is frequent for a frail elderly patient to develop a low-grade bronchopneumonia during the course of X-ray treatment.

Every means should therefore be taken to eliminate all septic foci in the mouth—teeth

cricoid. It is not always possible to determine operability until the pharynx is opened. If after opening the pharynx it does not appear possible to perform a conservative excision a pharyngolaryngectomy may be done with the first stage of reconstruction of the pharynx and the formation of a permanent tracheotomy.

Some details of the successful cases deserve comment. In the first place all 5 epilaryngeal cases had involvement of cervical glands. In 4 the gland dissection was done at the same time as the pharyngotomy and in 1 four weeks before. The experience of this small series certainly lends no support to the opinion that if glands are involved radical operation is not worth attempting. In 3 cases the pharynx was closed by primary suture and in 2 a fistula was made and closed at a second stage. In spite of these successes with primary closure, Trotter's final opinion was that a fistula should always be made at the first operation as a safeguard against sepsis.

In 1932 Trotter published 6 other cases of survival without recurrence for five years or more—the longest being twenty years so that from one hospital we have knowledge of 13 successful radical operations. When one considers the perseverance of surgeons in other fields such as cancer of the œsophagus and lung it is surprising that so little is being attempted for cancer of the pharynx. The greatest obstacle to success in the past was infection, and in penicillin and sulphonamides we have the means of controlling this risk. In addition to chemotherapy there have been advances in the knowledge of anaesthesia and nutrition which should further increase the margin of safety. The time is ripe for surgeons to apply these new resources to the surgery of cancer of the pharynx and to make fresh efforts to treat this distressing disease.

Gwen Hilton: *Carcinoma of the pharynx.*—In the Radiotherapy Department of University College Hospital during the years 1942 to 1946 inclusive, 89 cases of pharyngeal growths were seen.

Of these 89 cases, 7 were considered too ill for any form of treatment, and 6 were treated by surgery alone.

One great difficulty in comparing the results of treatment of cancer of the pharynx is that of the exact diagnosis of the site of the growth. In most of the cases seen, the growth was so advanced that the whole of one side of the oro- or hypopharynx was involved. A growth which is confined to the pyriform fossa or aryepiglottic fold, or a tonsillar growth which has not invaded the neighbouring tissues, is rarely sent for radiotherapy. Sometimes, however, as the growth shrinks under treatment, it is possible to be fairly certain of its actual site of origin. The cases have been divided up into those having growths arising in the oropharynx, the hypopharynx and the post-cricoid region. There were 16 cases with growths in the oropharynx, 63 cases with growths in the hypopharynx and 10 cases with growths in the post-cricoid region. To give an idea of the extent of the primary growth they have been divided into two stages: Stage I included cases in which the growths were confined to the tissue of origin. Stage II included cases in which the growths had become diffuse and spread from their point of origin to involve other pharyngeal structures.

Only 13 cases of the whole 76 were included in Stage I. The remaining growths were Stage II. It was surprising to find that no glands were palpable in 17 Stage II cases although the primary had involved the whole or part of one side of the oro- or hypopharynx. In 25 of the Stage II growths, however, there were large masses of matted glands in the neck.

It is seen from this that most of the growths were advanced. They are a discouraging group of cases, only a small number of them offering even a chance of cure.

The usual duration of symptoms before the patient was first seen was three to four months, but a few patients gave quite long histories of twelve to eighteen months, and this raised the average duration of symptoms to six months. The duration of symptoms in cases with widespread growth was usually short, suggesting that in advanced cases the progress of the disease was more rapid from the beginning. A biopsy was done in 73 of the 89 cases. All the 16 cases where no biopsy was taken were advanced, and there was no doubt as to the clinical diagnosis. All the hypopharyngeal growths from which a biopsy was taken were squamous carcinomas, except one, in which parts of the section suggested a lympho-epithelioma.

The growth in the hypopharynx of one case which was demonstrated at the meeting was a fibrosarcoma. It was not included in this series, as the treatment was only carried out in 1947. The immediate response of this tumour to irradiation was good. The biopsies of tumours arising in the oropharynx showed not only the more usual squamous carcinomata, but also some tumours of lymphatic origin, under which term are included the reticulocell sarcomata, the lymphosarcomata, &c.

The histological picture before treatment did not always help in the prediction of the response to irradiation. Histologically identical growths may respond differently to irradiation according to the tumour bed from which they arise. For instance, one sees cases of

Section of Pædiatrics

President—W. G. WYLLIE, M.D., F.R.C.P.

[February 27, 1948]

MEETING HELD AT GUY'S HOSPITAL, LONDON

Coarctation of the Aorta in the Neonatal Period.—C. W. KESSON, M.R.C.P.

In spite of the fact that coarctation of the aorta is not uncommon and that the defect is present at birth, few cases have been reported in infancy and none appears to have been published where the diagnosis has been made in life in the neonatal period.

The following case is of interest in that manifestations were present enabling a clinical diagnosis to be made on the fourth day of life, and the diagnosis was confirmed at post-mortem, when the child was 4 months old.

G. W., male aged 4 months.

The second child of a mother who has mitral stenosis, due to recurrent rheumatic infection in childhood. Her first child, a boy now aged 6½, is reported to be perfectly well.

During this pregnancy extra periods of rest were prescribed and she was throughout under close observation, but no indication for the termination of pregnancy developed.

On 28.9.47 the child, who weighed 5 lb. 9 oz. was delivered naturally, at full term. There was no dyspnoea or cyanosis. Breast feeding was instituted and sucking was satisfactory. On 2.10.47, when 4 days old, cyanosis developed after feeding and on crying.

The baby was not dyspnoeic but general cyanosis developed on crying. Forcible pulsation was observed in the neck and also in both axillary and brachial arteries. The whole course of the axillary and brachial arteries was clearly demarcated on the two sides.

The blood-pressure was equal in the two arms: systolic 125 and diastolic approximately 90, but sounds audible to zero.

The blood-pressure in the legs could not be determined. No pulsation could be detected in either femoral artery.

There was cardiac enlargement, rate 160, regular rhythm, no murmur was audible. No finger clubbing, no evidence of collateral circulation.

Chest X-ray: Heart shadow occupied three-quarters of the thorax. No rib notching.

On the evidence of (1) Abnormally forcible pulsation in the arteries of the arm and neck; (2) raised arm blood-pressure; (3) absence of pulsation of the femoral arteries; (4) cardiac enlargement, a diagnosis of coarctation of the aorta was made.

Progress.—The baby had difficulty in obtaining an adequate food intake from the breast and complementary feeds of half-cream national dried milk were given from the 10th day. At 12 days the cyanosis was persistent, associated with an increased respiratory rate (70) and heart-rate of 170. There was no pyrexia and no change in the physical signs. Breast feeding was abandoned. Oxygen was administered with relief of the cyanosis.

Gradual improvement occurred, the cyanosis again becoming intermittent, the heart-rate falling to 130 and the respiratory rate to 40. There was a slow erratic gain in weight to 6 lb. 15 oz. and the baby was discharged on 13.12.47, the cyanosis having completely subsided. Slow progress was continued at home until 1.2.48 when he developed an upper respiratory tract infection. On 3.2.48 he became worse, refusing his feeds; there was dyspnoea and the cyanosis had recurred. On 4.2.48 he was readmitted to hospital gravely ill with bronchopneumonia, which proved fatal within twenty-four hours. At this time (age 4 months) he weighed 9½ lb.

should be removed and infected gums treated. Penicillin either in the form of lozenges, sprays or injections should be employed to deal with the infection on the growth itself. We often spend a week or more dealing with the infection before beginning irradiation, and find the time well spent.

In addition the general condition should be improved as much as possible. The cancer patients having radiotherapy require the same careful general treatment as do those having, for example, a partial gastrectomy. The medical and nursing care of the patient before and during the treatment is most important. Since the growth frequently causes great difficulty in swallowing, the patient is often thin, wasted and anæmic from lack of adequate nourishment. If solids cannot be swallowed, a high calorie fluid diet must be given, and the vitamin content must be considered. If the patient cannot take adequate nourishment by mouth, a gastrostomy must be considered. This should be carried out before the treatment is begun, since it is unwise to interrupt a course of irradiation in the middle. Similarly, if a tracheotomy is indicated, it should be performed before beginning treatment. Any anæmia should be treated by full doses of iron, and in some cases by transfusion. The progress of patients often depends on building up their blood.

During the course of the treatment there is bound to be a severe reaction of the mucous membrane of the throat if adequate irradiation is given—and the patient will then need most careful nursing. Much can be done to alleviate the pain and soreness in the throat by giving tablets, such as benzocaine tablets, to suck before meals, or benzocaine emulsion to sip during the meals and aspirin sprays and gargles in between.

What benefit has the radiotherapy been to the patient? 15 out of the 71 cases which had a complete course of X-ray treatment are alive now. The average duration of life of the 71 patients was 18.4 months. The average duration of the 15 patients who are alive now is 36.6 months. The longest survival in this group so far is five years eight months. The growth in this case was confined to the epiglottis. It is interesting to note that the 3 cases in which the growth was confined to the epiglottis and aryepiglottic fold are alive. The longest survival period is five years eight months, the second four and a half years and the third two and three-quarter years.

The prognosis of the tumour of lymphatic origin, such as the lymphosarcomata and reticulum-cell sarcomata, which have infiltrated the surrounding tissues, appears to be better than the carcinomata when these have spread beyond the tissue of origin. One of the patients in whom the tumour had spread from the tonsillar fossa on to both pillars of fauces, the soft palate and down the pharyngeal wall has so far lived four years three months, despite the infiltration of the surrounding tissues. The section showed a stem-cell sarcoma.

The average duration of life of 18.4 months may not show a great prolongation of life, but I do not think one should only consider the duration of life of the patient when one is trying to assess the benefit which may be derived from any form of treatment; but one should also consider whether palliation is achieved and whether the patient is free from pain and able to work. We have only considered the disease to have been palliated by treatment when both the primary growth and the enlarged glands in the neck have undergone at least 50% diminution in size, when the patient's symptoms have improved sufficiently for him to say that he really feels better and able to work, and has gained weight. In quite a large proportion of the cases we did achieve palliation, but in a number it was short-lived, especially in many of the 25 cases which had a huge projecting mass of matted glands in the neck. The treatment in these cases was a failure because the improvement was so short-lived. The average duration of life in these 25 cases was only 7.7 months. The mass of glands in the neck was greatly reduced in size, but a hard residuum usually remained which sooner or later caused severe pain, almost impossible to relieve. Only very occasionally did the matted masses of glands resolve completely. In such cases with extensive secondary masses in the neck, therefore, it does require considerable judgment to decide whether or not radiotherapy is worth while.

There is a second category in which this decision may also be difficult. That is when clinical cachexia is prominent and when the sepsis in the throat does not clear up with preparatory treatment. In the first place irradiation is never successful in the presence of uncontrolled sepsis and, in the second place, it is difficult to prevent lung infections which are apt to be fatal. Real palliation was, however, achieved in many of the remaining cases. Unfortunately one can rarely say beforehand from the clinical examination, plus the plain histology, that is without special cytological counts, whether or not the treatment will be successful.

Lieut.-Colonel W. L. Harnett, [Medical Secretary to the Clinical Cancer Research Committee of the British Empire Cancer Campaign, contributed statistics showing the results of treatment in 511 cases of primary pharyngeal cancer, in which the survival rate in each stage of the disease was compared with the five-year expectation of life. It is hoped that this contribution will appear in full in the *Journal of Laryngology and Otology*, together with a complete report of the meeting.

had a normal arm blood-pressure in the neonatal period. Finally there is evidence that a raised pressure may become further elevated, at any rate during the period of growth (Steele, 1941; Campbell and Suzman, 1947).

The present evidence leads one to the conclusion that although a raised arm blood-pressure may occur in the neonatal period, this is not invariable and it may prove to be unusual but the exact frequency must await the collection of further data from cases investigated at this period of life.

Campbell and Suzman (1947) show that forcible pulsation of the arteries of the neck is a common manifestation; in the cases reviewed by Rhodes and Durbin (1942) it was more frequently commented upon in those over 10 years old but it was this feature which first aroused suspicion in the present case.

Eisenberg (1938) expressed the opinion that absent or feeble femoral pulsation was the simplest and most direct method of making the diagnosis. This is supported by the fact that of the 34 cases where this examination was recorded, femoral pulsation was absent in 24 and in 10 only feeble pulsation was detectable (Rhodes and Durbin, 1942). The absence of femoral pulsation was an essential part of the diagnostic evidence in the present patient.

Although the demonstration of a collateral circulation by clinical or radiological methods is of great diagnostic help in the older age-groups, they have rarely been present in children under 6. Rooke (1938) records a child of 3 in whom a collateral circulation was demonstrable clinically but there was no erosion of the ribs. Neuhauser (1946) reports the presence of rib notching at the age of 19 months.

The present evidence suggests that these manifestations are unlikely to be of help in the youngest age-groups.

Præcordial murmurs can do no more than raise suspicion of the diagnosis. The murmur heard in the interscapular space is more important. No murmur was ever audible in the present case. Cyanosis will occur in those cases where the descending aorta is entirely dependent on a patent ductus arteriosus for its blood supply, as the result of complete occlusion of the aorta proximal to the site of the insertion of the ductus arteriosus. In the present case the cyanosis was almost certainly pulmonary in origin and probably due to atelectasis secondary to the enormous cardiac enlargement. The reasons for this statement are that the cyanosis was immediately relieved by the administration of oxygen, and it was completely absent from the age of 2 months until the terminal bronchopneumonia at 4 months.

Conclusions.—Evidence is already available to suggest that not all cases of coarctation of the aorta will present features enabling a diagnosis to be made in the neonatal period. It is, however, considered that more cases would be recognized if palpation of the femoral pulse became part of the routine medical examination and if coarctation of the aorta was considered in all cases with cardiac murmurs or where there was a forcible pulsation in the neck arteries.

I wish to acknowledge my indebtedness to Dr. P. R. Evans, and also to the Department of Medical Illustration at Guy's Hospital for the drawing of the specimen.

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Post-mortem (Dr. Keith Simpson) 5.2.48.—Deep cyanosis was present in the lips and at the nail beds; the ankles and feet were also (more generally) cyanosed. No clubbing of the fingers. There was considerable enlargement of the heart (weight 54 grammes). The pericardium was normal. The left ventricular wall measured 1.4 to 1.6 cm. The endocardium and muscular wall of the left auricle was also markedly thickened though neither cavity was appreciably dilated. Both septa were normal and the foramen ovale was functionally closed and largely adherent from thickening of the auricular endocardium. The ductus arteriosus was closed, the dimple of the site alone remaining on both pulmonary and systemic aspects. Constriction of the aorta occurred at the termination of the aortic arch immediately distal to the origin of the left subclavian; at the point of maximum narrowing the intima was slightly wrinkled and thickened and the lumen reduced to 0.6 mm. No obvious collateral circulation was established and there were no other vascular anomalies (see fig. 1).

The common iliac arteries appeared hypoplastic, but in fact compared equally in diameter with those of 3 other children of between 3 and 5 months who were seen during the succeeding five days.

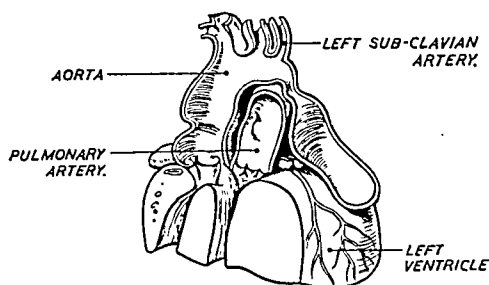


FIG. 1.

Respiratory system.—The upper respiratory tract was filled with œdema fluid tinged with blood, and this was further complicated by the addition of thin pus in the lower bronchial tract, the mucous membrane of which was inflamed by recent suppurative bronchitis. Patches of coarse collapse were present throughout both lungs, no part being affected more than another, and there was some general congestion, but neither to a marked degree.

There was no evidence macroscopically of pneumonia.

Routine examination, including the brain, revealed no further abnormalities.

Comment.—Campbell and Suzman (1947) have enumerated the cardinal clinical features in coarctation of the aorta as follows: (1) A raised blood-pressure in the upper half of the body. (2) Forcible pulsation of the arteries of the neck. (3) Feeble or absent pulsation in the femoral arteries and the abdominal aorta, and a low blood-pressure in the legs with a high or relatively high pressure in the arms. (4) The collateral circulation shown round the scapulæ, on the side of the chest wall, and over the anterior abdominal wall. (5) The collateral circulation shown by notching of the ribs on X-ray examination. (6) A systolic murmur (rarely with a thrill) at the base of the heart and often in the back, sometimes with a diastolic murmur.

It is generally agreed that, with rare exceptions, the blood-pressure in the upper half of the body is raised. Lewis (1933) stated: "It may seem natural to assume that if high pressure is found in the adult case, it has been present continuously from the first year of life; actually experience shows that assumptions of the kind are not without danger."

Although we still lack adequate records covering the younger age-groups, a raised pressure has usually been recorded at the initial examination (King, 1937; Steele, 1941; Rhodes and Durbin, 1942). The present case shows that this raised pressure may occur even in the neonatal period.

Cases of coarctation of the aorta have been described where the arm blood-pressure was normal (Blackford, 1928; King, 1937; Bramwell, 1947). Other cases have had a normal pressure which has become elevated during the course of time (Farris, 1935; Schwartz and Tice, 1939). It is reasonable to assume that these cases would have



FIG. 1.—Proptosis, ectropion and obstructed nose. December 1947.



FIG. 5.—Proptosis, ectropion, obstructed nose and right fronto-temporal metastasis. January 1948.



FIG. 2.—Lateral X-ray of normal shows clear nasopharyngeal airway (A) and soft palate (B) in usual position.



FIG. 3.—Lateral X-ray of patient's skull shows obstructed nose and nasopharynx (A) and depression of soft palate (B).

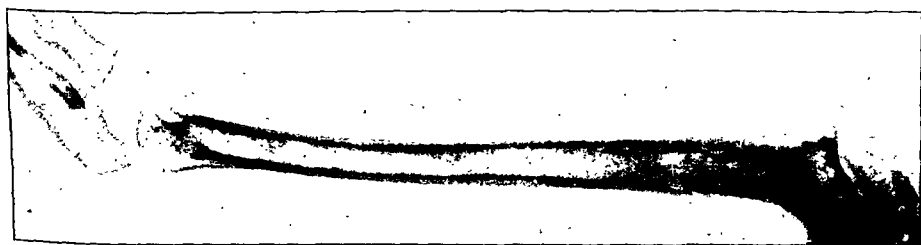


FIG. 4.—X-ray of right humerus showing metastasis.

Malignant Nasopharyngeal Tumour with Exophthalmos.—D. G. VULLIAMY, M.B.
C. B., aged 4 years.

The child was quite well until whooping cough July 1947.

August 1947: Slight trauma to left knee after which tenderness of lower third of femur developed with pyrexia. Blood culture: *Staph. aureus*. Acute osteomyelitis diagnosed at Dartford County Hospital. X-ray of femur then normal and pyrexia responded to penicillin. "Glazed look" of eyes noted by parents at this time (? onset of blindness).

September 1947: Onset of drowsiness, anorexia, headache and gradually increasing exophthalmos. Deterioration of vision in right eye.

October 1947: Increasing blindness, spreading to left eye. Optic atrophy in the right, papilloedema of the left. Thought to have retro-orbital neoplasm but radiotherapy not carried out owing to poor ultimate prognosis.

November 1947: Exophthalmos subsided and general condition improved. Blindness remained. Nasal discharge—right side.

December 1947: Admitted to Guy's Hospital. Afebrile, good appetite, able to play happily with toys. Some exophthalmos of right eye (fig. 1) and oedema of conjunctivæ. Slight exophthalmos of left eye. Perception of light only in both eyes. *Discs*. Bilateral optic atrophy. Exaggeration of deep reflexes in legs, ankle clonus, bilateral extensor plantar responses and absent abdominal reflexes. Tenderness over long bones especially tibiæ. Blood-stained nasal discharge from right nostril. Palpable swelling in nasopharynx with some depression of palate.

X-rays.—*Skull* showed progressive rarefaction of bone in nasal region and obstruction of nasopharyngeal airway (fig. 2 normal, fig. 3 patient). *Long bones*: Small areas of rarefaction (e.g. 2 mm. by 3 mm.) particularly at ends of bones, increasing in size later (fig. 4).

Blood picture: Hypochromic anæmia only. No abnormal white cells. *C.S.F.* normal. *Serum cholesterol* 100 mg. %. *Biopsy of tumour* in nasopharynx—an undifferentiated round-cell tumour, ? sarcoma, ? neuroblastoma. *Tibial puncture*: Needle entered secondary deposit and smear showed mass of similar small round cells. *Sternal puncture*: Normal marrow.

Course.—January-February 1948 (fig. 5). Exophthalmos again increased. Hard rounded swelling appeared in skull (right frontal region) extremely radiosensitive. No further radiotherapy given, however, on account of metastases. General condition deteriorated with remissions and death occurred on 26.2.48.

Autopsy.—Tumour 7.5 cm. by 10 cm. by 7.5 cm., apparently arising in the nasopharynx and growing up through the floor of the middle cranial fossa involving body and wings of sphenoid, and destroying optic nerves. Pressure atrophy of base of brain in this region. Small deposit 3 cm. diameter in frontal bone (R.). Infiltration of cervical lymph glands both sides. Wedge-shaped hæmorrhagic deposits in cortex both kidneys.

Microscopy showed that tumour consisted of uniform mass of small round cells resembling lymphocytes. Deposits in lymph glands and kidneys consisted of similar cells. Tonsils showed malignant hyperplasia. Suprarenals normal.

Comment.—This case presented an interesting diagnostic problem. The illness began with slight trauma to the leg followed by local pain and pyrexia, which was diagnosed as osteomyelitis; such an onset is described as occurring in "Ewing's tumour" of bone, and many of the subsequent features fitted well with Ewing's clinical description, including the nature of the spread.

According to Willis (1948), however, the majority of Ewing's tumours are not primary tumours of bone but secondary deposits usually from suprarenal neuroblastomata.

occurred while penicillin was being given) produced viscid mucopus. One stertorous breath taken through mouth for each 8 to 12 inspiratory efforts per minute. Sucking-in of lower ribs and suprasternal and submandibular regions. Orthopnoëic. Fed on expressed breast milk by pipette three-hourly.

November 21, 1947: Probe passed into nostrils met bony obstruction at 1 inch on either side. Breast feeding exhausted child after five sucks. Alternate tube and bottle feeds. Baby collapsed in asphyxial attack in which respiratory efforts reached 80-100 per minute. Revived in oxygen tent when tongue pulled forward.

December 4: Lipiodol X-ray of nose showed obstruction. Nasal discharge less after this. At times three or four consecutive breaths through mouth. Changed from breast milk to half-cream Cow and Gate.

January 21, 1948: (Esophageal feeds abandoned. Breathing through mouth much more easily.

February 27: Very well. Satisfactory weight gain (fig. 1). Breathing through mouth but with some effort.

Bilateral Choanal Atresia.—L. F. W. SALMON, M.B. (for R. J. CANN, M.S.).

CASE II.—Female aged 18 months. Seen at St. Helier Hospital, by Mr. R. J. Cann, within a day or two of birth, the complaint being intermittent asphyxia and difficulty with sucking.

Diagnosis.—Bilateral choanal atresia.

It was decided to treat her conservatively, and she was seen again at Guy's at 6 months old, when she was gaining weight and managing well. At her next visit, three months later, she was having difficulty with taking solid food, and it was decided to admit her.

Admitted on her first birthday, but no surgical treatment undertaken for three months.

Operation, on 9.10.47, under general anæsthesia. Both diaphragms were broken down and found to be membranous. The child was breathing through her nose within forty-eight hours of operation, and has remained well since.

Bilateral Choanal Atresia.—L. F. W. SALMON, M.B. (for R. J. CANN, M.S.).

CASE III.—Female aged 15 years. Admitted when 2 days old under Mr. W. M. Mollison with the complaint that she could not suck, and that she became cyanosed when the mouth was closed.

Diagnosis.—Bilateral congenital choanal atresia.

Operation nine days after admission.

Without anæsthetic a labyrinthine gouge was passed through each side of the nose in turn and an opening made through the obstructing diaphragm on each side. The diaphragm was bony.

The patient's condition was at once improved and she was discharged a week after operation. She was readmitted once or twice in the next six months and once more recently for the apertures to be enlarged.

Dr. Philip Evans: This rare congenital anomaly (fig. 2) interests the pædiatrician primarily as a cause of neonatal asphyxia; it is well to remember that in the newborn child "the nostrils are the proper channel through which respiration takes place, that breathing through the mouth is an unnatural accomplishment learned afterwards" (Ronaldson, 1881, *Edin. med. J.*, 26, 1035). The difficulty may have been exacerbated in Case I by micrognathia. The key to the diagnosis is that there is inspiratory recession in the submandibular region as well as of suprasternal tissue and the lower part of the thorax, i.e. the obstruction is above the level of the glottis. The intermittent manner in which the obstruction (due to the apposition of tongue and palate) is overcome is also characteristic. The consistency and position of the post-nasal plates may be gauged by probing, while lipiodol dropped into the nostrils provides an elegant radiological demonstration of the lesion.

In the present case the striking remission of symptoms and subsidence of the exophthalmos would also have been consistent, as these tumours are known to retrogress occasionally.

The section from biopsy material and the puncture of the secondary deposit in the tibial marrow would both have supported the diagnosis, as the typical rosette formation of neuroblastomata is frequently absent in young subjects.

No primary suprarenal tumour was, however, found and only the final histological examination of autopsy specimens demonstrated the diagnosis of primary lymphosarcoma of the nasopharyngeal lymphoid tissue.

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CLINICAL DEMONSTRATION AND PAPER.

The Indications for Surgery in Congenital Heart Disease.—J. M. H. CAMPBELL, O.B.E., M.D.

CLINICAL DEMONSTRATIONS.

Brachydactyly—A New Family.—E. B. DAWE, M.R.C.S. **Ganglioneuroma and Pes Cavus.**—D. Q. TROUNCE, M.B. **"Epituberculosis."**—L. G. SCOTT, M.B. **Epiloia and Eventration of Diaphragm.**—S. A. MARSH, M.R.C.S. **Thyrotoxicosis.**—F. S. MELLOWS, M.R.C.S.

MUSEUM SPECIMENS AND DEMONSTRATIONS.

Errors of Upper and Lower Incisor Relationships.—R. E. RIX, M.R.C.S., L.D.S. **Infanticide.**—C. KEITH SIMPSON, M.D. **Teeth: Neonatal Line and Hypoplasia.**—M. A. RUSHTON, M.D., L.D.S. **Congenital Obstructions of Alimentary Tract.**—J. K. MARTIN, M.B. **Siamese Twins.**—R. C. MAC KEITH, M.D. **Prevention of Infection in Neonatal Ward.**—J. B. BLAICKLEY, F.R.C.S., and F. A. KNOTT, M.D. **Infant's Laryngoscope and Inclined Table, and Tracings of Respiration in Infants.**—G. F. GIBBERD, M.S., and J. B. BLAICKLEY, F.R.C.S.

Bilateral Choanal Atresia.—PHILIP RAINSFORD EVANS, M.D.

CASE I.—Female aged 15 weeks. Born November 14, 1947: blue asphyxia, mucus aspirated and baby placed in oxygen tent where she was kept for five days. Much mucus removed from pharynx and from nose, proteus infection of the latter (which

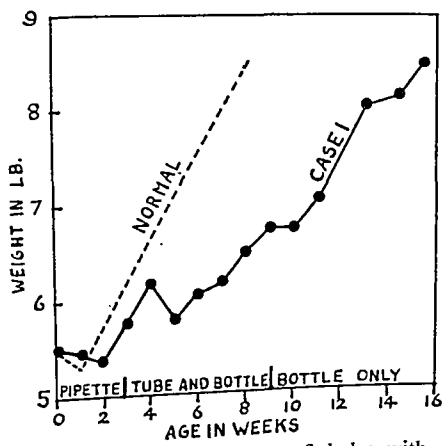


FIG. 1.—Weight chart of baby with congenital choanal obstruction. (Case I.)

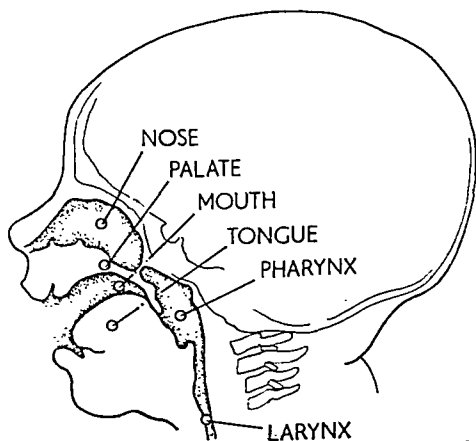


FIG. 2.—Diagram showing structural block between nose and nasopharynx and functional block between mouth and oropharynx. (From radiograph of the child at 3 weeks.)

occurred while penicillin was being given) produced viscid mucopus. One stertorous breath taken through mouth for each 8 to 12 inspiratory efforts per minute. Sucking-in of lower ribs and suprasternal and submandibular regions. Orthopnœic. Fed on expressed breast milk by pipette three-hourly.

November 21, 1947: Probe passed into nostrils met bony obstruction at 1 inch on either side. Breast feeding exhausted child after five sucks. Alternate tube and bottle feeds. Baby collapsed in asphyxial attack in which respiratory efforts reached 80-100 per minute. Revived in oxygen tent when tongue pulled forward.

December 4: Lipiodol X-ray of nose showed obstruction. Nasal discharge less after this. At times three or four consecutive breaths through mouth. Changed from breast milk to half-cream Cow and Gate.

January 21, 1948: Œsophageal feeds abandoned. Breathing through mouth much more easily.

February 27: Very well. Satisfactory weight gain (fig. 1). Breathing through mouth but with some effort.

Bilateral Choanal Atresia.—L. F. W. SALMON, M.B. (for R. J. CANN, M.S.).

CASE II.—Female aged 18 months. Seen at St. Helier Hospital, by Mr. R. J. Cann, within a day or two of birth, the complaint being intermittent asphyxia and difficulty with sucking.

Diagnosis.—Bilateral choanal atresia.

It was decided to treat her conservatively, and she was seen again at Guy's at 6 months old, when she was gaining weight and managing well. At her next visit, three months later, she was having difficulty with taking solid food, and it was decided to admit her.

Admitted on her first birthday, but no surgical treatment undertaken for three months.

Operation, on 9.10.47, under general anæsthesia. Both diaphragms were broken down and found to be membranous. The child was breathing through her nose within forty-eight hours of operation, and has remained well since.

Bilateral Choanal Atresia.—L. F. W. SALMON, M.B. (for R. J. CANN, M.S.).

CASE III.—Female aged 15 years. Admitted when 2 days old under Mr. W. M. Mollison with the complaint that she could not suck, and that she became cyanosed when the mouth was closed.

Diagnosis.—Bilateral congenital choanal atresia.

Operation nine days after admission.

Without anæsthetic a labyrinthine gouge was passed through each side of the nose in turn and an opening made through the obstructing diaphragm on each side. The diaphragm was bony.

The patient's condition was at once improved and she was discharged a week after operation. She was readmitted once or twice in the next six months and once more recently for the apertures to be enlarged.

Dr. Philip Evans: This rare congenital anomaly (fig. 2) interests the pædiatrician primarily as a cause of neonatal asphyxia; it is well to remember that in the newborn child "the nostrils are the proper channel through which respiration takes place, that breathing through the mouth is an unnatural accomplishment learned afterwards" (Ronaldson, 1881, *Edin. med. J.*, 26, 1035). The difficulty may have been exacerbated in Case I by micrognathia. The key to the diagnosis is that there is inspiratory recession in the submandibular region as well as of suprasternal tissue and the lower part of the thorax, i.e. the obstruction is above the level of the glottis. The intermittent manner in which the obstruction (due to the apposition of tongue and palate) is overcome is also characteristic. The consistency and position of the post-nasal plates may be gauged by probing, while lipiodol dropped into the nostrils provides an elegant radiological demonstration of the lesion.

In Case I breast and bottle feeding were exhausting. Nutrition was maintained, but no more, by pipette feeding. When alternate feeds were given by œsophageal tube the infant gained weight; the tube was used until the baby was 9 weeks old.

Dr. P. Evans showed a colour film made by Dr. Brian Stanford of the normal relationship of sucking and breathing in a healthy baby, and followed it with one of Case I, made by Mr. Eric Gwynne-Evans.

Mr. E. Gwynne-Evans: The movements of an infant are not so haphazard or aimless as might be supposed. By studying the movements of foetal sheep that had been isolated in a warm saline bath (Barcroft) and the movements of non-viable as well as viable foetuses in man (Gesell) it has been shown that they are the forerunners of movements necessary to preserve existence after birth. In fact, the viability of a prematurely born infant is dependent upon these movements being sufficiently well developed to support life independently of the maternal circulation.

The movements of muscles in breathing and feeding appear early and are deeply ingrained in the make-up of the newborn infant. They are more or less stereotyped in form; Gesell describes them as "survival patterns" and they are universal to all. This film demonstrates three main features of the newly born infant's equipment: the firmly established and insistent rhythm of the respiratory musculature; the automatic "patterning" of the oro-facial muscles in sucking and the dependence of the infant on a free nasal airway.

In both the acts of sucking and nasal breathing, soft tissue profile radiographs have shown that the posterior part of the tongue and the soft palate are closely applied to one another. This "patterning" of the palato-lingual musculature shuts off the oral cavity from the nasopharyngeal airway, and is so deeply ingrained within an infant's make-up that in this infant with congenitally obstructed posterior nares, prodigious efforts are made by the respiratory musculature to overcome the obstruction.

Consequently, when the infant is at rest, the ratio between efforts to breathe through the nasal passages and the mouth, is about eight to one, and the cyclical attacks of partial asphyxia which occur are relieved mostly by crying. During the act of sucking, the inspiratory efforts result in gross indrawing of the epigastrium, intercostal spaces, supraclavicular triangles and the submandibular tissues, until eventually a stage of asphyxia is reached and is relieved by oral breathing.

In this particular case, the indrawing of the intercostal spaces suggested an obstruction of the airway, but as Dr. Evans pointed out, it was the indrawing of the submandibular tissues that indicated the site of the obstruction to be above the larynx.

With regard to the future, when sucking is no longer the predominant method of feeding, it will be easier for the tongue to fall away from the palate; the lips will tend to remain apart, and mouth-breathing proper will supervene. It has been noticed, however, that in these special circumstances the ability to mouth-breathe has been acquired at an earlier date, i.e. before the time when sucking is replaced by spoon feeding.

Mr. L. F. W. Salmon: The treatment of cases of bilateral congenital choanal atresia presents many difficulties. The rather less rare cases of unilateral atresia, although calling for attention later in life, are not the same grave problem and, of course, are usually not seen by the pædiatrician.

Dr. Evans has drawn a graphic picture of the precarious nature of the first months of life in the bilateral cases. That these manage to survive, however, even in the absence of the correct diagnosis, is borne out by recently published figures (Durward, Lord and Pelsen, 1945). Of 46 established cases, 11 were first referred for a surgical opinion between the ages of 21 and 45, and 17 between 11 and 20.

Dr. Evans has discussed the nursing and management of these cases. The arguments against postponing operation revolve round the risks the infant must then face, e.g. asphyxia, inanition, sinus infection and its complications, pulmonary infections or atelectasis.

The arguments against early operation are: (1) The danger of surgical procedures in the first days of life. (2) The danger of an operation on the airway of a sick baby, and (3) The technical difficulties.

I believe that as long as the child continues to thrive and put on weight, the operation should be postponed, if possible, until at least the end of the second year.

REFERENCE

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Brains from Streptomycin-treated Cases of Tuberculous Meningitis.—G. PAYLING WRIGHT, D.M., and R. J. W. REES, M.B.

The brains and spinal cords from the first three fatal cases of tuberculous meningitis treated with streptomycin at this Centre (Guy's Hospital) were exhibited as

gross anatomical specimens. The patients were all young children between 2 years 6 months and 2 years 10 months, who had been admitted for treatment. All had received streptomycin for at least eight weeks before death.

CASE I.—B. M., male, aged 2½ years.

Admitted May 31, 1947, with three-week history of increasing drowsiness, weakness and fits. Diagnosis confirmed; intramuscular and intrathecal streptomycin commenced June 7 for nine weeks, condition deteriorated and he died in coma 18.8.47.

Autopsy showed primary tuberculous complex of left lung; no miliary tuberculosis. Thrombosis of longitudinal sinus; small tubercles along Sylvian fissures; a thick gelatinous basal exudate. Considerable degree of symmetrical hydrocephalus; a large caseous tuberculoma in choroid plexus of left lateral ventricle.

CASE II.—M. H., male, aged 2 years 10 months.

Admitted November 15, 1947, in a semiconscious state. Diagnosis confirmed, and intramuscular and intrathecal streptomycin given for eight weeks. Died in coma January 22, 1948.

Autopsy showed primary tuberculous complex of right lung; a few inactive miliary lesions in spleen and liver. Marked yellow basal exudate particularly in interpeduncular fossa; severe symmetrical hydrocephalus with a few small tubercles in choroid plexus.

CASE III.—G. T., male, aged 2½ years.

Admitted June 8, 1947, with short history of facial weakness, spasticity of legs and marked nystagmus; diagnosis confirmed. Intramuscular and intrathecal streptomycin given for eight weeks. Stopped because of very poor condition. Remained in coma and died January 18, 1948.

Autopsy showed primary tuberculous complex of right lung; no miliary lesions in body. Thick basal exudate and very severe hydrocephalus.

These cases were demonstrated to show what we considered at that time to be important changes that develop after prolonged but unsuccessful treatment. The findings have been fully supported in the recent report on tuberculous meningitis treated with streptomycin (Report of Tuberculosis Trials Committee of the Medical Research Council, *Lancet*, 1948, i, 582).

The base of each brain was covered by a thick, yellowish and gelatinous exudate, most marked in the interpeduncular fossa. Ziehl-Neelsen films prepared from these basal exudates contained very large numbers of acid-fast bacilli morphologically resembling typical tubercle bacilli. Cultures from the material confirmed them to be tubercle bacilli of human type and all sensitive to streptomycin (0.25 to 0.5 mg. streptomycin per ml.), identical in sensitivity to the cultures obtained before treatment with streptomycin. Despite the very large number of tubercle bacilli present in the basal exudate at autopsy, the C.S.F. during life had shown a progressive falling off in numbers of organisms seen in direct film and subsequent culture, 2 cases having a sterile C.S.F. during the last two and four months of life respectively.

The brains had been cut coronally to display the lateral ventricles. All 3 showed a symmetrical hydrocephalus of considerable degree, in Case III the cortex measured only 0.5 to 0.75 cm. in thickness, with flattening of the convolutions and narrowing of the sulci. One of the cases was fully investigated during life (Case II) and found to have a hydrocephalus of the communicating type. The choroid plexuses of the lateral ventricles contained several small tubercles and in Case III a tuberculoma measuring 1 cm. in diameter.

Case I showed three foci of gross nodular thickening of the dura opposite the lumbar intervertebral spaces, which on section proved to be non-tuberculous, probably traumatic, granuloma associated with the very large number of lumbar punctures made.

Miliary Tuberculide of Skin.—RONALD MAC KEITH, D.M.

B. V., male, born 4.10.42.

On 20.8.47 sudden onset of breathlessness and fever; sent to hospital as acute anterior poliomyelitis, but found to have miliary tuberculosis and transferred to Guy's Hospital.

27.8.47: Acutely ill, dyspnoëic, respirations 60 to 90. X-ray chest showed miliary shadows. No choroidal tubercles at this date and on 7.9.47 streptomycin treatment (0.2 grammes I.M. six-hourly) started and continued to present date. His general condition has steadily improved.

16.9.47: Many tubercles present in choroid. Since then these have been gradually resolving. Before admission the cerebrospinal fluid contained 7 lymphocytes per c.mm. From October there was a gradual rise till on 10.12.47 there were 192



FIG. 1.—Skin of palms (photograph taken 3.5.48).

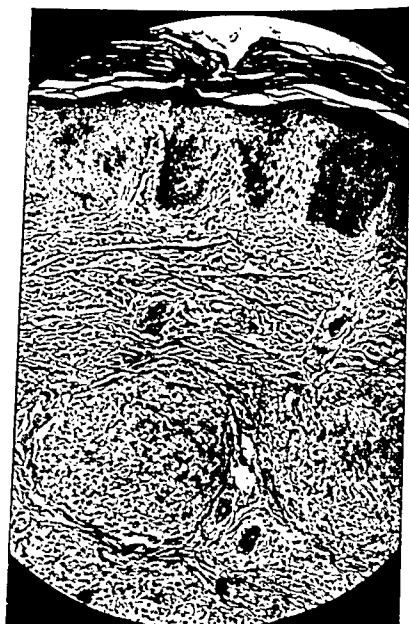


FIG. 2.—Section of a lesion ($\times 65$).

lymphocytes and 20 polymorphs, but since then these have fallen to 16 lymphocytes and 1 polymorph. By November 1947 the lung fields had become clear. About this time dusky red papular lesions up to 8 mm. diameter, some with necrotic centres, gradually developed. These (fig. 1) are very gradually diminishing. Biopsy examination of a lesion showed a histological picture consistent with a diagnosis of miliary tuberculide of the skin (fig. 2).

POSTSCRIPT.—In June 1948 these skin lesions were still present, having only slightly diminished.

[April 23, 1948]

Acute Infantile Hemiplegia**PRESIDENT'S ADDRESS**

By W. G. WYLLIE, M.D., F.R.C.P.

ACUTE INFANTILE HEMIPLEGIA needs to be defined. The term has been in use since the middle of the nineteenth century to denote certain cases of hemiplegia of sudden tempestuous onset in children, of a few weeks to 6 or more years of age. The outcome may be quickly, or gradually, lethal; there may be permanent hemiplegia with mental impairment, or slow, though often only partial, recovery; or, most interesting of all, rapid and complete restoration to normal health with no repetition of the convulsive assault.

My material consists of 7 cases of acute infantile hemiplegia, 6 encountered within the last twelve months—which shows it as a not uncommon condition—and 1 older case with rapidly fatal issue, added because of its complete histological investigation. 5 boys and 2 girls, with ages between 11 months and 4 years; 5 with spontaneous onset, 1 complicating mumps and whooping cough, and the seventh due to a tuberculoma. Of the 7, 2 were rapidly fatal, 1 gradually fatal, 2 made a rapid, and 2 a gradual, recovery.

The aetiology is still speculative, though some hard facts have emerged. At least we know that the same clinical picture may be produced by many different causes and cover a variety of anatomical lesions.

Between 1840 and the 1920s, the output of writing on the subject grew prodigiously, chiefly in collecting cases and theorizing on their causation. Interest then abated and since the 1920s only a few thorough studies of the pathology of individual cases have been added. Recently, speculation has been busy on the aetiology of the paralyses, sometimes bilateral, sometimes unilateral, complicating the infectious fevers, especially of the demyelinating type. A new lead has been given by experimental pathology to the study of the demyelinating encephalopathies. The subject of infantile hemiplegia at least deserves discussion, even if much further clarification is needed.

The clinical picture.—The onset of acute infantile hemiplegia is always spectacular. The description given by Dr. James Taylor serves as well to-day as when he wrote it in 1905. He said, “a child, hitherto healthy, suddenly becomes ill without any apparent cause, between the ages of 1 month and 6 years. The early symptoms are severe, and consist of convulsions, fever, often vomiting, and always coma”. The convulsive element may be lacking, especially in the post-exanthematous cases, and, without it, irritability and stupor pass into coma. Two-thirds of all infantile hemiplegias, Taylor stated, were ushered in by convulsions. These symptoms persist for twenty-four hours to a week, and, during this period, or as consciousness returns, it is apparent that a hemiplegia is present, affecting the face, the arm, and lastly the leg. “The limbs remain flaccid for some days, after which the flaccidity begins to lessen, and the limbs become spastic. In some cases the paralysis completely disappears.”

To my mind, the hemiplegia fully developed has some resemblance to that produced by the apoplectic stroke in the arteriosclerotic adult, where a massive and sudden vascular catastrophe occurs in the territory of the middle cerebral artery. The uselessness of the arm exceeds that of the leg; the facial weakness tends to disappear first. There the similarity ends. As Taylor said, the commencement of infantile hemiplegia has no parallel in the adult hemiplegia. Further, the anatomical lesions are dissimilar.

In addition to the cases of apparently spontaneous eruption, one must add, as Taylor remarked, that in about a third of the infantile hemiplegias the disease appears as a complication of one of the infectious fevers. Even in 1905 he added, and I think this equally important to-day, there was no obvious connexion between the specific

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FIG. 1.—Skin of palms (photograph taken 3.5.48).

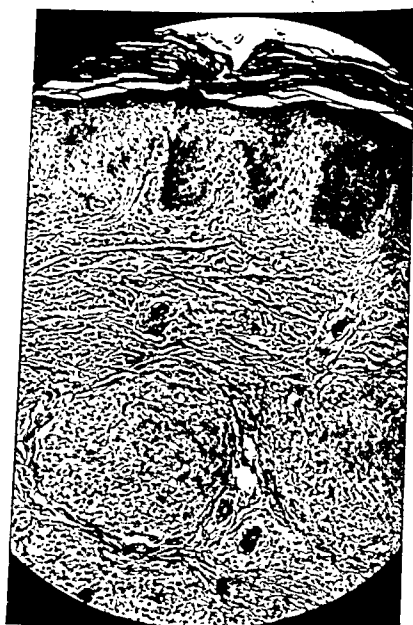


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lymphocytes and 20 polymorphs, but since then these have fallen to 16 lymphocytes and 1 polymorph. By November 1947 the lung fields had become clear. About this time dusky red papular lesions up to 8 mm. diameter, some with necrotic centres, gradually developed. These (fig. 1) are very gradually diminishing. Biopsy examination of a lesion showed a histological picture consistent with a diagnosis of miliary tuberculide of the skin (fig. 2).

POSTSCRIPT.—In June 1948 these skin lesions were still present, having only slightly diminished.

hemiplegias of antenatal and natal origin, however, are in existence from birth and only a small percentage of such cases are epileptic. I have nothing more to say about them except that abnormal labour is an important ætiological factor in the congenital group of hemiplegias (23%).

Also difficult to differentiate from a case of acute infantile hemiplegia is the infant of good bodily health and nutrition, which, at a few weeks or months of age, commences to have a series of little fits or twitchings, or severer convulsions perhaps affecting one-half of the body, and accompanied very often by temporary want of movement of a limb or limbs. To a trained observer, such an infant may always have aroused suspicions of a want of interest or intelligence. Pneumoencephalography is the only method I know whereby the poverty of one or both hemispheres, in all the crudity of their maldevelopment, or possibly natal damage, can be revealed beyond dispute (fig. 1).

To return to the morbid anatomy of infantile hemiplegia, R. M. Stewart's cases are a selective group of hemiplegias with mental deficiency of institutional domicile. It is not always known when the amentia first declared itself, as at time of certification the parents' statements are often unreliable.

TABLE III.—(R. M. STEWART, 1947) HEMIPLEGIAS: AGE AT ONSET

	Male	Female
Congenital	15	21
During 1st year ..	19	25
During 2nd year ..	10	7
During 3rd year ..	1	4
During 4th year ..	1	2
During 5th year ..	3	3

It will be noted that the majority, or 102 cases, male and female, were either congenital or occurred in the first three years of life. Many of these hemiplegias with onset after birth must have depended on natal or antenatal defects, although in some the hemiplegia was ushered in by convulsions soon after birth. 3 cases are of special interest with onset of convulsions and hemiplegia within the first two years of life, as they showed at autopsy sometime before their thirtieth years *hypoplasia* of one hemisphere. The small hemisphere showed no reduction in size of nerve cells, no vascular changes, no gliosis, no atrophy of convolutions, no widening of sulci. It must have been due to a developmental error in fetal life (fig. 2).

Speculation on autopsy material from patients dying years later than the onset of the hemiplegia is of limited value, as gliosis or scar-tissue will have blurred out the original traces. Multiple confluent petechial hæmorrhages, or necrotic areas due to asphyxial venous congestion at birth, may coalesce and lead to a large trabeculated cystic cavity in the central white matter of one hemisphere (fig. 3), or an initial softening with disappearance of cortical neurones may gradually be replaced by a secondary sclerosis or gliosis, ending in *lobar sclerosis*, or even *hemiatrophy* of the brain. Taylor held the view that as a result of vascular occlusion in childhood atrophy and shrinkage without death of the supporting tissues was a possibility (fig. 4).

Norman, from his study of these delayed forms of birth palsy in mental defectives at Stoke Park Colony, Bristol, aptly remarks that the original lesions spare sufficient cortical tissue to mask for the time being the inherent instability of the infant's motor apparatus. But as sclerosis gradually increases, epileptogenic foci are formed, convulsions begin, and hemiplegia is precipitated.

A common combination of central softening and secondary sclerosis, along with *état marbré* of the basal ganglia, accounts for the frequency of some degree of athetosis in the affected limbs of some young hemiplegics; infantile hemiplegia differing in this aspect from the adult form. The explanation lies in the lesions being in the territory of venous drainage of the great vein of Galen in the infantile form. As Eardley Holland showed, the venous tributaries draining the central white matter of the hemispheres are end-veins stopping short of the cortex, but having the corpus

fever and the complicating, though rare, hemiplegia. The method of association is still a matter of controversy. Possibly it is unwise to concentrate too rigidly on a conflict in one hemisphere, as both may be affected, either spontaneously, or following one of the specific fevers. The bilateral involvement then produces a diplegia, though often of unequal severity in the two halves of the body.

The following tables give some idea of the frequency of hemiplegia to diplegia; age of onset; and spontaneous onset as opposed to being a complication of a specific fever. These tables were compiled by notable physicians in the more spacious days of the past. Sachs and Peterson (1890) show the greater frequency of hemiplegia to

TABLE I.—SACHS AND PETERSON

Age onset	Hemiplegia	Dipl.	Para	Total
Congenital ..	22	20	7	49
1st year ..	27	1	2	30
2nd year ..	17	1	—	18
3rd year ..	16	2	1	19
4th year ..	4	—	—	4
5th year ..	4	—	—	4
6th year ..	2	—	—	2
7th year ..	1	—	—	1
8th year ..	5	—	—	5
9th year ..	—	—	—	—
10th year ..	—	—	—	—
Under 15 ..	4	—	—	4
Not known ..	3	—	1	4
Total	105	24	11	140

diplegia, and that 82 of the hemiplegias are contained in the congenital group and in those noted to have arisen in the first three years of life. Table II gives the records

TABLE II.—ACUTE INFANTILE HEMIPLEGIA

	Freud	Osler	Taylor
(Congenital) ..	(76)	(15)	(—)
1st year ..	162	45	19
2nd year ..	139	22	16
3rd year ..	81	14	3
4th year ..	36	1	3
5th year ..	26	3	1
6th to 10th year ..	75	10	—
Total	519*	95†	42

* Includes infectious fever cases. † 16 after infectious cases.

collected by Freud (1897), Osler (1889), and Taylor (1905). Freud's list contains hemiplegias from every conceivable source; Osler's, only 16 as complications of infectious fevers, and Taylor restricted his to such cases as are of apparently spontaneous onset. In all, the great preponderance in the first three years of life is clearly indicated. Gowers (1888) stated that seven-eighths of acute infantile hemiplegias had their onset in the first five years of life.

With the concentration of cases within the first three years, it is probable that many of those which suddenly develop hemiplegia of a permanent character, and are associated with mental deficiency, depend on antenatal and especially natal causes. The trigger that fires the explosion, the convulsion and hemiplegia, is not pulled, however, until some time after birth. In many of this type a history of prolonged, difficult labour and asphyxia of the infant at birth is obtained.

Before reviewing the morbid anatomy of acute infantile hemiplegia, and before looking for the reason of the delayed onset of hemiplegia of natal origin, the ground must first be cleared of some of the so-called congenital hemiplegias.

This is not always easy, as it may be several months before a unilateral weakness becomes obvious. Most of the activities of the newborn infant depend on reflex pathways in the brain-stem and spinal cord, and signs of pyramidal involvement of a higher level take a variable time to appear. Parents are unaware of any fault until their suspicions are aroused by the infant's retarded power of action. Most

A picture of unilateral sclerosis and cystic degeneration, probably of vascular causation, is depicted in figs. 5 and 6, from a case published by W. E. Le Gros Clark and Dorothy S. Russell (1940, *J. Neurol. Psychiat.*, 3, 123). It shows the shrivelled left hemisphere from a girl, previously in good health, who, at 8 years, suddenly became convulsed and developed an acute hemiplegia, and after some general improvement died at 13 years in a condition resembling status epilepticus. Here there was a conspicuous degree of atrophy and cystic degeneration of the left cerebral

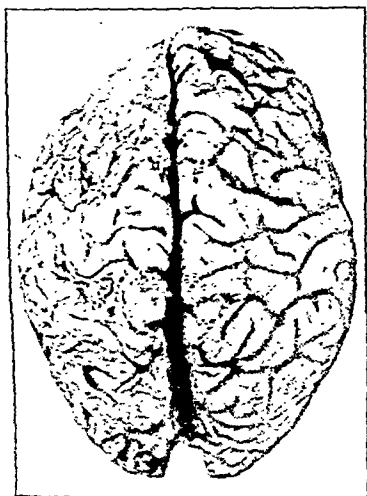


FIG. 5.—Left lobar sclerosis, probably of vascular origin, in case of acute hemiplegia at 8 years (by courtesy of Professor Dorothy Russell).



FIG. 6.—Ventricular dilatation and cortical cystic degeneration.

(Figs. 5 and 6 are reproduced by permission of the Editor of *J. Neurol., Neurosurg. Psychiat.*)

cortex, with advanced demyelination and gliosis of the white matter of that hemisphere. There was no resemblance to Schilder's encephalitis. Two similar examples have been recorded by Bielschowsky.

The morbid anatomy of "acute infantile hemiplegia" as defined by Taylor, where the earlier history provides no suspicion of mental or physical defect, appears to depend almost entirely upon vascular changes, not in the form of gross bleeding or rupture of vessels, but in the form of vascular occlusions, arterial more often than venous, either by embolism or thrombosis; or in perivascular changes due to agents, toxins, and other antigens travelling via the blood-stream.

The anatomical lesions show great variety. In rapidly fatal cases, arterial occlusion is a common finding. Whether it be embolism or thrombosis is disputed. In 1 of my 7 cases, a child just under 2 years, in good health, suddenly developed convulsions, coma, right hemiplegia, and died within a week. At autopsy, the left anterior cerebral artery was occluded throughout its distribution. On cross section, the left frontal lobe showed a multitude of minute black vascular points. There was no disease found in the circle of Willis, nor in any other part of the body.

Ford and Schaffer (1927) record 16 cases with vascular occlusions, usually in the territory of the middle cerebral artery.

In some cases with previous good health coming to autopsy soon after the onset of hemiplegia, two types of encephalopathy have been described. The first appears to be a non-specific acute toxic encephalopathy occurring in many different diseases, probably as a result of bacterial toxins. Grinker and Stone have described the lesions varying from congestion, œdema, necrotic nerve cells and disintegration of cortical neurones to areas of cortical softening. Proliferation of the endothelium of the small cerebral vessels was observed, but an absence of signs of bacterial invasion. With lesions sufficiently extensive, a hemiplegia or diplegia may be produced. In cases of

striatum within the same venous system. With difficult prolonged birth and severe head moulding, the vein of Galen is kinked on the straight sinus and severe asphyxial congestion, œdema, diapedesis of red cells affect the central areas of the hemispheres and the basal ganglia. In the adult hemiplegia, the damage is in the arterial pathway, middle cerebral artery usually.



FIG. 1.—Occipito-posterior presentation, prolonged labour, asphyxia at birth. Twitchings, chiefly left-sided, from second month. Lumbar encephalogram at 7 months: cortical atrophy and ventricular dilatation.



FIG. 3.—Cystic cavity, false porencephaly: breech birth, hemiplegia of sudden onset at 2 months (R. M. Stewart's case).

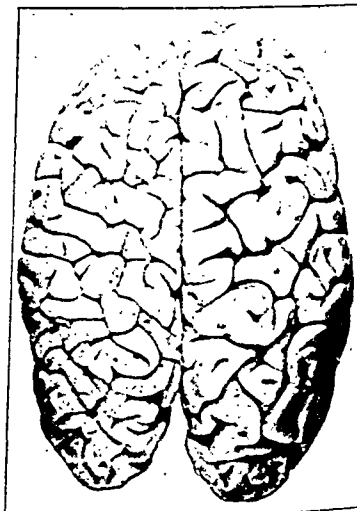


FIG. 2.—Right hemiplegia acquired in second year; patient died aged 29, epileptic and mentally defective (R. M. Stewart's case). Hypoplasia left hemisphere.

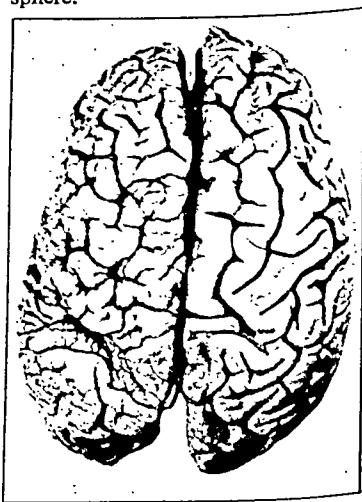


FIG. 4.—Lobar sclerosis, hemiatrophy left hemisphere; congenital hemiplegia (R. M. Stewart's case).

One of my cases was probably of the above type; a boy born with some asphyxia and head moulding developed, in July 1947, a sudden convulsive episode with acute right hemiplegia and mental impairment. He improved for a time, but later grew worse and died in December of the same year. The C.S.F. had been normal. In November, Mr. McKissock had performed a lumbar encephalogram, which showed gross bilateral cortical atrophy with dilatation of the ventricles. The left cortex opposite the hemiplegia was more atrophic than the right.

Strümpell (1884), later supported by Marie (1885), that infection was the cause, and the infection probably polio-encephalitis, the counterpart of poliomyelitis. This must finally be abandoned. Recent research by Howe and Bodian in man and chimpanzee refers to the minor encephalitis accompanying the spectacular myelitis, meaning that the cerebral lesions lack the saturation of the spinal ones. Barring the brain-stem nuclear lesions causing most of the deaths in acute infantile paralysis, there is no authentic instance known of hemiplegia, nor of diplegia, due to the virus of polio. The initial stage of stupor, or of coma, seen in some cases of polio is ephemeral.

(2) A theory based on more solid ground is that of vascular occlusion, usually arterial, either by embolism or thrombosis. Some acute hemiplegias undoubtedly occur as a result of an infectious fever. I have mentioned those in diphtheria with cardiac weakness. Rolleston was able to collect in 1908 66 cases complicating scarlet fever, and in 6 out of 7 post-mortems embolism or thrombosis was found to be the cause. But this does not provide an answer why a child in apparent good health may suddenly be convulsed, become comatose, and show a hemiplegia. Yet in one of my cases already mentioned, the anterior cerebral artery on one side was thrombosed.

(3) More recently, other viruses, type unknown, are used as scapegoats to explain all cerebrospinal paralyses of obscure origin. There is little evidence to support this theory in regard to a permanent hemiplegia, or a diplegia. Viruses are selective, with preference for the nuclear masses of grey matter. In epidemic encephalitis, the preference is for nuclei in the brain-stem, and hemiplegia is an uncommon expression of this disease. Recovery from virus invasion of nuclear cells, also, is slow and often incomplete, so would not account for sudden hemiplegia with rapid recovery.

(4) In the third of all the acute infantile hemiplegias reckoned to follow the acute infectious diseases, I have already mentioned the non-specific encephalopathies, acute toxic and hæmorrhagic, which have been found in some cases. These it is thought are secondary processes to circulating bacterial and other toxins. No doubt on a grand enough scale, one or other type might produce a hemiplegia; or an acute cerebellar ataxia, if the vascular lesion is in the cerebellum.

(5) Lastly, there is the group of encephalopathies complicating vaccination, variola, measles, chicken-pox, rubella. In them the nervous complications are varied, but a hemiplegia or a bilateral paresis, temporary or permanent, has often been witnessed. In some cases the onset is spontaneous—acute spontaneous encephalomyelitis. In both the post-exanthematous and the spontaneous, the histological lesion is essentially the same. The characteristic anatomical lesion is perivascular demyelination in the central white matter of the hemispheres.

So far, no theory of how the demyelination is produced has stood its ground. At first, either the virus of the exanthem was accused, or a hypothetical neurotropic virus activated by the primary infection. Demyelination, however, is not a proved feature of virus infection in man, nor in the experimental animal, nor is it found as a result of generalized vaccinia. The secondary virus remains hypothetical and has escaped detection.

Recently, a more promising line of investigation into the production of demyelination is being perfected by the experimental pathologist. Briefly, this is the production of multiple lesions of demyelination in monkeys and other animals by injection, subcutaneously or intramuscularly, of homologous or heterologous white brain substance, combined with adjuvants, heat-killed acid-fast bacilli, &c. The adjuvants help to precipitate the reactions, but the injection of the adjuvants alone produced no results. This reaction is considered to be an immunological tissue response, or one due to allergy, or a specific brain antibody-antigen reaction. The similarity to the lesions in some of the post-infectious encephalopathies in man is considerable, and it is suggested that an infecting agent may stimulate formation of a cerebral

minor severity the damage is reversible and recovery may be gradual. This type of encephalopathy, as also the second type, is chiefly a complication of pneumonia, tonsillitis, scarlet fever, and other acute infectious diseases.

The second type sometimes found is called the hæmorrhagic encephalopathy. In this, as a result of bacterial or other circulating toxins (Alpers, 1928), small areas of congestion and necrosis surrounding small blood-vessels, which may have their lumen occluded by swollen endothelium, are found chiefly in the white matter of the brain. The circular areas are usually ringed by a hæmorrhagic zone. There is no evidence of bacterial invasion. Similar lesions may be produced following treatment with arsenical compounds.

The toxic and the hæmorrhagic encephalopathies are distinct anatomically from the type characterized by demyelination in the central white matter. In the latter form convulsions may be an initial symptom, but more often stupor sinks into coma. Hemiplegias, diplegias and other nervous signs occur in this type of encephalopathy, and may be either temporary or permanent.

It is, perhaps, necessary to state that gross or macroscopic hæmorrhage, intracerebral, is one of the rarest intracranial lesions in childhood. None of the cases presented was secondary to disease elsewhere in the body. So intracranial bleeding secondary to leukaemia, hypertension, bacterial endocarditis, spontaneous sub-arachnoid hæmorrhage, can be excluded. Nor were they due to diphtheria with severe cardiac involvement and dislocation of clot from the auricles.

Despite the excellent description of subdural hæmatoma in children from birth onwards by Ingraham and Matson, who collected 98 cases in six and a half years, I have, in the last two years, after diligent search by dural taps in all infants under 6 months in my ward with suspicions of cerebral disturbance, so far only found one in twenty examinations with a subdural hæmatoma. The condition occurs more often in children under 2 years of age, due to injury to the head. 2 recent ones I have had were in toddlers after an injury to the head from a fall. The bulging fontanelle, torpor, punctate hæmorrhages in the fundi, facilitated the diagnosis. One had extensive unilateral subdural clot, with contralateral paresis of the limbs, and

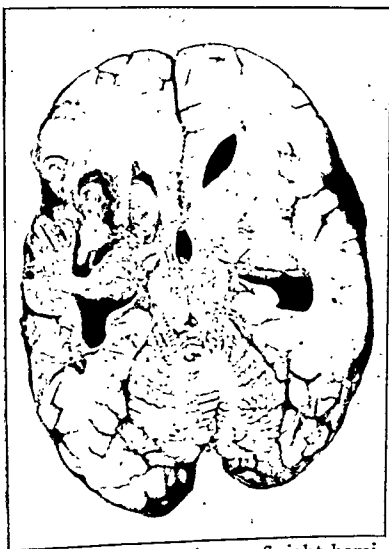


FIG. 7.—Tuberculoma of right hemisphere; left hemiplegia of sudden onset.

the other a large right cephalhæmatoma, fractured parietal bone, and gross underlying extradural extravasation, and mild paresis of the left arm. Nor should we expect the extradural or subdural hæmatoma to give rise to hemiplegia, unless the blood clot be excessively thick and extensive. The infant's cortex withstands an amazing amount of pressure without focal paralysis appearing. Paralysis, hemiplegia, is more likely to appear later as a result of atrophy of the cortex.

Only one other instance of confusion shall I cite; a boy of 1 year and 3 months, who developed a convulsion lasting four hours, followed by frequent twitching, fever, and a left hemiplegia. The optic fundi were normal. Mantoux skin reaction was strongly positive. X-ray of chest revealed miliary tuberculosis. At autopsy an enormous tuberculoma impinging on the right internal capsule was found, which had produced no inconvenience until convulsions occurred (fig. 7).

Theories of pathogenesis of acute infantile hemiplegia.—The pathogenesis of acute infantile hemiplegia I have reserved to the last. A review of the voluminous literature clearly shows how speculation has outrun fact.

(1) Of historical interest is the theory, so long-lived and widely accepted, of

Strümpell (1884), later supported by Marie (1885), that infection was the cause, and the infection probably polio-encephalitis, the counterpart of poliomyelitis. This must finally be abandoned. Recent research by Howe and Bodian in man and chimpanzee refers to the minor encephalitis accompanying the spectacular myelitis, meaning that the cerebral lesions lack the saturation of the spinal ones. Barring the brain-stem nuclear lesions causing most of the deaths in acute infantile paralysis, there is no authentic instance known of hemiplegia, nor of diplegia, due to the virus of polio. The initial stage of stupor, or of coma, seen in some cases of polio is ephemeral.

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antigen which reacts with specific antibody in perivascular tissues (Morgan, 1947; Kabat *et al.*, 1947).

The hypothesis is attractive, but can as yet only be advanced tentatively. Hurst (1944), working experimentally on demyelination, stated that the means by which it can be produced are diverse; further, its production under experimental conditions does not necessarily furnish a clue to the ætiology of those human diseases characterized by perivascular demyelination.

Such a theory, however, would go far to explain some of the cases of spontaneous hemiplegia and diplegia in childhood. Short of demyelination, which is irreversible, there is perivascular œdema and exudate. The process need not progress to its full development, and recovery can be expected. In 3 of my list of hemiplegias, 1, a child of 3 years and 10 months, developed acute infantile hemiplegia and was fully recovered in three months. In two others, with spontaneous hemiplegias coming on at 11 months and at 17 months of age (one being under the care of Dr. M. Edmunds), recovery has been almost complete, except for a slight clumsiness of the affected hand, in periods of three months and one year respectively. Such cases surely cannot be ascribed to vascular thrombosis, and are unlikely complications of virus invasion. The cerebrospinal fluid was normal in each. In a similar connexion I may mention a post-measles case of Dr. Sheldon's, a boy of 8½ years, exposed to measles beginning of April 1947, eight days later was given 5 c.c. measles convalescent serum, with subsequently a mild attack of measles. Seven days later he became drowsy, febrile, comatose, diplegic, but in eight days was completely well again. Even more suggestive was a case I saw of a girl of 7½ years, who, eight days after a normal vaccination, became irritable, stuporose, febrile and rigid, with bilateral extensor plantars, yet within five hours she was conscious, able to feed herself, and her spasticity had departed. To my mind, such cases speak, not for a bacterial agent, but for a specific tissue reaction, possibly antigen-antibody acting through vascular channels, and in these several instances, arrested in an early stage before irreversible damage had occurred. One last case, which I may mention through the kindness of Dr. Banks of the Park Hospital, a boy of 4 years had concurrently whooping cough and mumps, and became convulsed, unconscious for six days, with a left hemiplegia clearing up in eight days. The pathogenesis is more controversial here, as the possible nervous complications of mumps are varied, but, as Dr. Taylor said many years ago, it is likely the specific fever stands only as a predisposing cause.

There is obviously much still to be done to unravel the pathogenesis of acute infantile hemiplegia and diplegia. The examination of pathological material calls for close study by the morbid anatomist as the opportunity occurs. The chances of further light being thrown on the problem, in my opinion, lie largely in the hands of the research worker in experimental pathology.

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Section of Proctology

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[January 14, 1948]

Thiersch's Operation for Anal Incontinence

By W. B. GABRIEL, M.S.

THIERSCH's operation consists of the insertion of a silver wire into the perianal space, so as to encircle and narrow the anus; it was described by Thiersch in 1891, and was devised originally as a method for treating rectal prolapse. The operation is clearly described in Kirschner's *Operative Surgery*, in Professor Hartmann's work on the *Surgery of the Rectum*, and in Carrasco's monograph, "*Prolapsus du Rectum*". The use of other materials such as silk, fascia, kangaroo tendon and rubber has been described for this operation.

So far as I am aware, Thiersch's operation has fallen into disuse, at any rate in this country during the present century, and the object of this communication is to indicate that Thiersch's operation still has a sphere of considerable usefulness and that in fact it may prove to be the operation of election in one of the most difficult and intractable rectal conditions which we encounter.

Indications.—Women who develop relaxation of the anal sphincters have for many years been a most difficult problem, particularly since the cause of the condition is usually undetermined.

Examination reveals a somewhat patulous anus which can be made to gape widely by digital traction. The normal anal canal appears to be absent and the rectal mucosa seems to come right down to the anal margin; this must be due, I think, to fatigue or loss of the normal motor innervation of the internal sphincter (lumbar sympathetic).

The tone of the external sphincter is variable; some patients can manage some voluntary contraction, but many of the old, deaf subjects have no voluntary contractile power. In all cases the resting tone of the external sphincter is poor and it becomes worse towards the evening after the patients have been up and about all day.

The chief symptoms are those of anal incontinence, with inability to hold flatus, and a variable amount of faecal leakage, always associated with the mental distress and uncertainty that might be expected. In addition there is often a mucosal prolapse sometimes amounting to a short complete prolapse.

Treatment in these cases has hitherto been very unsatisfactory. Faradism sometimes helps a little but is often disappointing. A ligature operation to remove the prolapsing mucous membrane is doomed to failure and recurrence if the sphincter remains relaxed.

Owing to the advanced age of many of these patients a minor procedure is most desirable, and it is in such cases that Thiersch's operation is indicated.

One further indication for Thiersch's operation is when the sphincter remains patulous after operation for a complete rectal prolapse. There was one such case in this series, a woman aged 52, for whom I had previously done a Moschcowitz operation; her extremely patulous sphincter showed little sign of improvement, and after an interval of six months the beginning of a recurrent mucosal prolapse became evident and I decided to carry out a Thiersch's operation as a supplementary procedure. This has given great relief and has prevented any further development of her trouble although she has subsequently broken her wire on two occasions. (Case mentioned later.)

Technique.—The operation is performed for preference under continuous pentothal, with the patient in the lithotomy position. Strict aseptic technique is necessary: the skin is carefully cleaned and prepared with tincture of iodine and a dry gauze swab may be tucked into the anal canal in order to prevent leakage of mucus. A soft, easily malleable silver wire, No. 19 or 20 S.W.G. is then passed round the anus in the perianal space through a skin puncture 1 inch posterior to the anus. Doyen's needle has proved to be ideal for this operation. The anal lumen allowed by the wire should be such as will pass a forefinger easily; the assistant keeps his finger in the anal canal while the wire is being twisted in order to guard against the wire becoming tighter during the twisting. The twist is made posteriorly and the wire is then cut, leaving about $\frac{1}{4}$ inch of the twist which is bent posteriorly towards the coccyx and then tucked well away into the subcutaneous tissues. The skin punctures anteriorly and posteriorly are closed with Michel clips.

Post-operatively the bowels are moved with the aid of a glycerin suppository or enema about the fourth day, and a good deal of care has to be taken for the next week or two to overcome a tendency to faecal impaction. The patients only need to be in bed for two or three days and there is very little pain after operation.

Results.—In 11 cases treated to date by Thiersch's operation the results have been, with

one exception, very satisfactory. The patients were all females; their ages ranged from 44 to 79, 4 being over 70. After insertion of the wire the patients have remarked on their comfort and feeling of security and the cases with prolapse have found this to be completely corrected. Moreover, after operation patients are perfectly well able to continue with their sphincter and levator contractions and in some cases I have noted an improved contractile power with the wire in position.

My first three operations of this nature were done with stainless steel wire (2 or 4 strands) and in two of these the wire subsequently broke, one after one month, one after three and a half months, and I re-operated on both cases, this time putting in a silver wire. One of the cases again broke her wire in the course of defaecation seven and a half months later; she knew at once what had happened and without delay returned with a view to its reinsertion; I did this under pentothal after removing the silver wire which was found to have broken on one side just beyond the twist. (Wires demonstrated.)

There has been one case of sepsis; the patient was a stout woman, aged 49, for whom I did a Thiersch's operation with silver wire under local anaesthesia. Six days later an acute ischiorectal abscess on the left side had to be incised; the abscess rapidly cleared up but two weeks later the wire was seen to be exposed, so I removed it under pentothal.

As to the duration for which the wires can be left, I am proposing to leave them indefinitely so long as the symptoms are relieved and no untoward incident develops. Four of these cases have retained the wire for six months (including the case previously mentioned who broke her wire after seven and a half months).

[A colour film of Thiersch's operation was shown.]

Recto-Sigmoidectomy for Complete Prolapse of Rectum

By MICHAEL J. SMYTH, M.Ch., F.R.C.S.

PROLAPSE of the rectum up to a distance of 2 in. involves all the coats of the rectum. Beyond this the prolapse usually involves the pouch of peritoneum on the anterior surface; in fact a prolapse of greater dimension is regarded by some surgeons as a sliding hernia of the rectum. The greater the prolapse the more is the rectovaginal or rectovesical pouch involved. Ernest Miles used to say that prolapse could not be greater than 6 in., but I recall a case of a boy aged 10 years admitted to hospital with a sudden prolapse which was almost 12 in. long. In this case there was an intussusception of the pelvic colon which had come through the anus drawing the rectum with it completely, so that there was no sulcus at the anal margin. It was necessary to open the abdomen to effect reduction.

The condition of complete prolapse of the rectum occurs more frequently in the later decades of life and much more frequently in women than in men, but recently I have seen cases in the middle thirties and forties. It may be that wartime and post-war diet may have led to some laxity of the tissues.

Many operations have been advocated for prolapse of the rectum, both intra-abdominal and extra-abdominal or perineal operations, but in my opinion recto-sigmoidectomy is the best method. Miles standardized the operation in his report to the Society in 1933 (*Proc. R. Soc. Med.* (1933), 26, 1445). Briefly it amounted to amputation of the prolapse, and an entrance to the peritoneal cavity was inevitable. Yet it was remarkable that before the use of sulphonamides and penicillin, with ordinary care peritonitis rarely, if ever, occurred. In Miles' review of 32 cases he reported only one death, and this was due to intestinal obstruction—a knuckle of small intestine being involved.

Nowadays preliminary treatment with sulphathalidine is given. The operation is done with the patient in the lithotomy position, the table being given a slight Trendelenburg tilt. With the surgeon seated he will find it an advantage to have the instruments on a small tray in front of him. The amputation should leave not less than 1 in. of bowel above the mucocutaneous junction. In this way damage to the external sphincter is avoided and sufficient bowel is left for anastomosis to the pelvic colon. I have seen 2 cases in which the sphincter had been destroyed completely. When the peritoneum is opened it should be well divided on both sides: the pelvic colon can then be drawn down to its full extent so that when it is divided there may be no slack left, thus ensuring against recurrence of prolapse. The peritoneum is then carefully closed and stitched snugly around the wall of the pelvic colon as high up as possible. The amputation is completed by dividing the pelvic colon obliquely from before backwards, the line of section being higher in front than behind. In this way the lumen of the colon will more closely approximate to that of the rectal wall and so make anastomosis easier. It is wise to spray the line of anastomosis with sulphonamide-penicillin powder before returning it through the anus, in fact the spray can be used at any time throughout the operation where the surgeon may think it necessary. Finally a medium-sized tube surrounded by gauze soaked in flavine and paraffin is inserted through the anus and kept in place by skin stitches.

In a series of 27 cases there was no death and one recurrence. This latter was due to the fact that the pelvic colon had not been divided high enough. In this case the patient had been given a spinal anæsthetic, and I agree with the view expressed by Mr. Gabriel that a general anæsthetic is better, as spinal anæsthesia brings about retraction of the pelvic colon, and so it cannot be divided as high as one would wish.

[A film of the operation in colour was shown.]

Anorectal Malignant Melanoma

By RONALD W. RAVEN, O.B.E., F.R.C.S.

A STUDY of the morphology and properties of the malignant melanoma leads us into a number of fields of investigation including the complex system of the sensory nerve-endings, the wide distribution of chromatophores and pigment formation in the animal kingdom. In addition, this is the most deadly of all known tumours. There is still much to be learnt concerning its properties and it is important to record isolated cases, especially of sites in the body where it is less frequently seen.

The type cell.—The type cell of the malignant melanoma is the melanoblast which is polygonal in shape, with short, hair-like processes and a vesicular nucleus with several nucleoli especially in the more malignant types (fig. 1). As the cell differentiates it becomes racquet-shaped, developing one or more stout cytoplasmic tails and, passing through a fusiform stage, it becomes an enormously elongated filamentous structure. Protoplasmic fibrils are found within the cells; in the benign type they are localized in the cell processes, but in the malignant forms they may run throughout the cell cytoplasm. Some of the cells

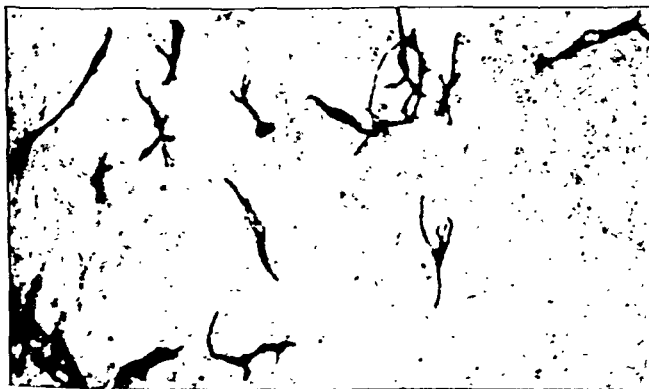


FIG. 1.—Melanoblasts in growing tissue culture of chicken embryo. This is the type cell of the melanoma ($\times 150$).



FIG. 2.—A melanoblast seen under a high microscopic magnification. The middle of the cell is occupied by the nucleus: the cytoplasm is filled up with pigment granules. This is an autonomous unit ($\times 1,200$).

contain a considerable amount of melanin, while many others are free from it. There is evidence that the presence or absence of melanin does not affect the malignant properties of the cell. The melanoblast is an active cell, moving among the fibroblasts by amoeboid movement, throwing out branches which are sometimes long and attached to the main body by a very thin thread. The melanoblast (fig. 2) is an autonomous unit, it possesses the properties for survival and can reproduce a new colony of cells.

It is also important to stress the tendency of melanoma cells to separate from the main

body of the tumour and be carried away to commence a new tumour colony in another locality of the body (fig. 3). The chance of an active cell becoming detached is very great and cytological studies prove that it occurs (fig. 4). The single cell is able to pass through the larger lymphatic channels and it becomes arrested in the fine filtering system in the liver, lung (fig. 5) or bone-marrow. When a group of cells detach themselves they are arrested in the regional lymph nodes. This property of producing widespread metastases is one of the

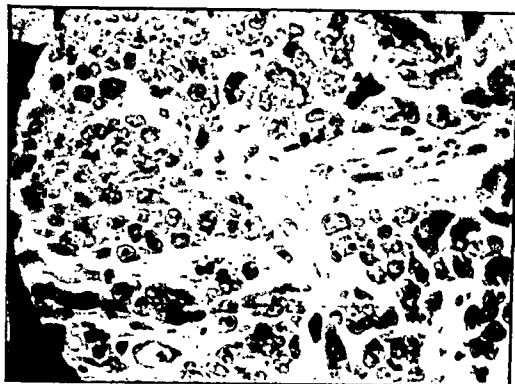


FIG. 3.

FIG. 3.—Cytological study of a melanoma in a dog showing an area with dividing tumour cells near the blood-vessels. The large number of blood-vessels and lymphatics in close contact with the tumour cells increases the possibility of widespread and distant metastases ($\times 700$).

FIG. 4.—Cytological study of a transverse section of an artery whose lumen contains melanoblasts, leucocytes and erythroblasts ($\times 350$).

FIG. 5.—Cytological study of a section of lung at autopsy. The individual tumour cells have been separated with a solution of acetic acid (strength 45%). The nucleoli within the nuclei of some of the cells are demonstrated ($\times 700$).

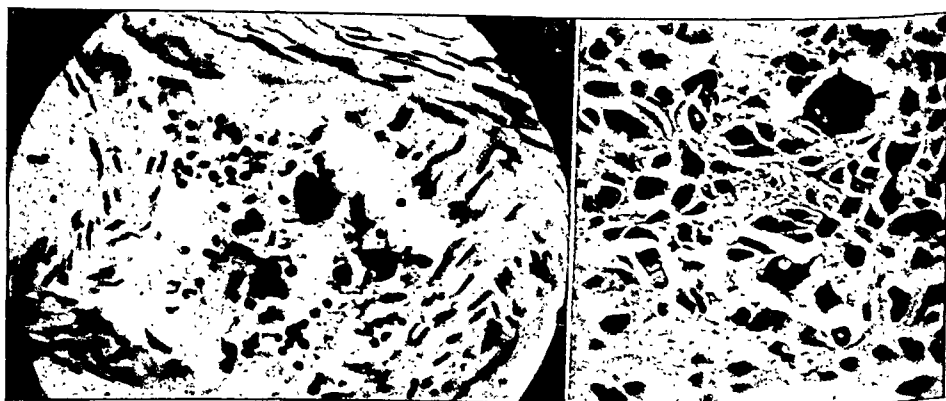


FIG. 4.

FIG. 5.

outstanding features of the malignant melanoma, and the patient usually succumbs, not as a result of the primary lesion, which may be a small nodule in the skin, but from generalized metastases.

TABLE I.—MALIGNANT MELANOMA. THE METASTATIC PICTURE

Lymph nodes	Lungs Heart	Liver Pancreas Omentum Bowel	Structures Involved			
			Brain	Generalized	Skeletal: Pelvis Femur Tibia Metatarsals Metacarpals	Skin: Multiple nodules

Incidence.—Malignant melanoma is not found frequently in the alimentary tract. In the œsophagus it is extremely rare and as far as I can ascertain from the literature only 3 cases have been reported. The stomach is affected infrequently but it is more common in the small intestine; thus in 1945 Herbert and Manges collected 25 cases in the literature; in 9 cases the tumour was considered to be primary and in 16 cases metastatic. It is infrequent in the colon.

The anorectal region is the commonest site in the alimentary tract to be affected by malignant melanoma but the total number of cases reported in the literature is not large. Over

one hundred cases have been reported. Miles stated that he had only seen 3 cases in a series of more than 1,500 cases of carcinoma of the rectum.

Case records.—During the past fifteen years I have only found the case-records of 3 patients admitted to the Royal Cancer Hospital and Dr. John Waugh informs me that only 10 cases have been seen at the Mayo Clinic.

CASE I.—Male, aged 59, was admitted to the Royal Cancer Hospital on December 6, 1933, under the late Mr. Cecil Rowntree, complaining of increasing constipation.

History.—For nine months the patient had experienced increasing constipation and a sense of obstruction in the rectum. Morning diarrhoea was present and "rectal prolapse" occurred which was diagnosed elsewhere as "piles". The stools were ribbon-like in character: no blood or mucus was present. He had lost 11 lb. in weight.

Examination.—Patient's general appearance was healthy. The abdomen was distended in the region of the cæcum. There were hard shotty lymph nodes in the left groin. A growth was present in the posterior wall of the anal canal filling the lumen, the lower limit extending down to the level of the white line. Bleeding occurred on examination.

Operation (Mr. C. Rowntree).—Exploratory laparotomy. Multiple nodules were found involving the small intestine, a small hard nodule was present on the vault of the urinary bladder and two large masses were found in the pouch of Douglas. The anal tumour was excised locally and diathermy applied to the base.

Histology.—"The tumour is a malignant melanoma, pigment formation is minimal. The growth is composed mainly of cells of epithelial type but in one part shows a tendency to spindle form. Small strands of necrotic squamous epithelium, a few tubular mucus-secreting glands and occasional unstriated muscle fibres are the only traces of tissue of normal structure in the specimen."

CASE II.—Male, aged 39, was admitted to the Royal Cancer Hospital on November 22, 1946, under Mr. R. C. B. Ledlie, complaining of rectal bleeding and discharge.

History.—For four months the patient had experienced severe bleeding and discharge from the rectum with incontinence of fæces. He had also noticed a lump at the anus and there was also loss of weight.

Examination.—Patient appeared to have lost weight. The abdomen was distended: liver not palpable. A swelling protruded from the anal orifice, 4 × 3 cm. in size, purplish in colour and of firm consistency. It extended high up the anal canal and induration of the ischio-rectal fossæ was present. There were several lymph nodes in both groins, firm in consistency. Radiological examination of the chest showed no abnormality.

Operation (Mr. R. C. B. Ledlie).—Exploratory laparotomy; Liver was normal: a large growth involving the rectum was found with extension to the right side of the pelvis. A left inguinal colostomy was performed. Excision of the rectum was not possible. Nineteen days later the protruding mass was excised by diathermy.

Histology.—"The tumour is a malignant melanoma. There is a partial covering of the tumour by squamous epithelium which is partly hyperplastic, partly atrophic and partly ulcerated. The malignant parenchyma shows considerable heterogeneity and many parts are completely achromic. Other parts show melanin pigmentation in both melanoblasts and chromatophores. The component cells are sometimes fusiform or polyhedral but there are many circumscribed lobulated masses of cells of large spheroidal form bearing a striking resemblance to certain neuro-epithelial end-organs. Mitotic figures and examples of nuclear hyperchromia, reduplication and syncytium formation are abundant and the tumour is extremely malignant."

CASE III.—Male, aged 62, was admitted to the Royal Cancer Hospital on March 9, 1933, under Mr. C. E. Shattock.

History.—For three months the patient had experienced pain on sitting down and had passed blood from the rectum for six weeks. No constipation. No pain on defæcation. Weight decreasing. Six weeks previously colostomy had been performed elsewhere.

Examination.—Abdomen: Liver not enlarged. Spleen and kidneys not palpable. A purplish-brown tumour was present occupying the anus, extending outward to the buttock and upward along the full extent of the anal canal. The mucous membrane of the rectum beyond the tumour appeared normal. Consistency firm and the tumour did not bleed.

Operation (Mr. C. E. Shattock).—March 16, 1933: Perineal excision of rectum. April 5, 1933: Excision of left inguinal lymph nodes.

Histology.—"Histology of the primary tumour is that of an actively growing, intensively pigmented, malignant melanoma. There is massive infiltration of the regional lymph nodes by malignant melanoma, but the highest node removed shows no invasion. Lymph node from groin—there is metastasis of malignant melanoma. There is massive invasion of the inguinal lymph nodes by malignant melanoma."

The patient subsequently developed suppression of urine and died on May 9, 1933. Autopsy showed septicæmia and pyelonephritis to be the cause of death. There was no evidence of metastases.

Site of Origin.—Usually the tumour arises in the anal canal or at the anal verge. It is very exceptional for it to commence in the rectum but such a case is described by Chaliér

and Bönnet where the tumour occurred in the rectum 6 cm. from the anal orifice. There is good evidence that the malignant melanoma arises in the skin of the anal canal and involves the rectum secondarily by direct extension. It is of interest also to note that Kallet and Saltstein have described a case of malignant melanoma arising in a rectal polyp. The posterior wall of the anal canal is more often involved than the others, followed by the lateral walls; the anterior wall is the most infrequent site.

The tumour usually forms a single mass, but a second smaller growth is sometimes present separated by apparently normal tissue. There may be a small anal tumour with a larger one in the ampulla of the rectum; or the primary tumour may be surrounded by a number of small satellites. The size of a malignant melanoma in this region varies from a miliary nodule to a large tumour, with many intermediate varieties.

Types of tumour.—There are two main types, namely sessile and pedunculated. It is a feature of the malignant melanoma in this region to become pedunculated and this explains the frequency with which it prolapses through the anal orifice. A case is described in the literature of spontaneous extrusion of such a tumour after detachment had occurred at its base. The base of the tumour is frequently mobile over the deeper layers of the anal canal. The tumour is usually lobulated and there may be areas of superficial ulceration present. It is frequently black in colour due to the presence of melanin, although an amelanotic type is described. The consistency is firm and elastic; sometimes it feels semi-fluctuant.

Spread of the tumour.

(a) *Direct extension.*—Malignant melanoma commencing in the anal canal shows a marked tendency to spread upwards into the rectum along the submucous tissues. It also spreads outwards into the cellular tissues surrounding the anus and rectum but this type of extension appears to be halted by the fibrous fascia propria of the rectum. Contrary to the behaviour of adenocarcinoma in this region, malignant melanoma does not usually invade adjoining structures such as the urinary bladder, vagina or sacrum. Nodules of growth may be found in the ischio-rectal fossa or in the cellular tissues in the hollow of the sacrum.

(b) *Lymphatic spread.*—Owing to the site of the primary growth, the inguinal lymph nodes are frequently involved; if only one lateral wall of the anal canal is affected, the lymph nodes on that particular side may be involved, the others being normal. It is worth noting that the inguinal nodes are sometimes enlarged and resemble a mild form of lymphadenitis without containing tumour cells. Further, it is necessary to distinguish between the presence of chromatophores in the lymph nodes and actual malignant melanoma cells. When the rectum is involved, its lymphatics are invaded as in the case of adenocarcinoma. Usually these metastases are black in colour, although the primary growth may be amelanotic. Involvement of the lymphatic system may be more generalized and includes the thoracic duct, mesenteric, mediastinal and submaxillary groups of nodes.

(c) *Hæmatogenous spread.*—Invasion of the blood-vessels leads to widespread metastases, but in certain cases, as in malignant melanoma of the eye, dissemination may be delayed for a considerable period of time. The liver is involved most frequently; it assumes a large size and is nodular. These nodules may be black or amelanotic. The peritoneum may be studded with neoplastic nodules and secondary deposits may be present in the small intestines, great omentum and appendices epiploicæ. The lungs and pleura are also involved frequently. The subcutaneous tissues, kidney, brain and meninges, pancreas, spleen and thyroid gland may be affected.

Symptomatology.—A common symptom of the disease is the presence of a protruding mass from the anal orifice which may be mistaken for a prolapsed thrombosed internal hæmorrhoid. Bleeding and discharge are frequently present. There may be irregularity of bowel action with frequency of defecation and tenesmus. The protruding tumour can be seen, and is dark brown or black in colour, or a nodular pedunculated mass can be felt in the anal canal, and a blackish discharge may be noted on the examining finger. The regional lymph nodes in the groin may be enlarged and somewhat tender. In advanced cases a large mass of nodes are present and ulceration with suppuration may occur.

It is necessary to distinguish the primary tumour from a prolapsed, ulcerated internal hæmorrhoid and if there is any doubt concerning the true nature of the swelling a histological examination should be made after biopsy.

Treatment.—The treatment of malignant melanoma of the anorectal region is by radical surgical excision. An exploratory laparotomy is carried out to determine the situation as regards extensions of the growth and its operability. When conditions are favourable an abdomino-perineal excision of the rectum and anus should be performed. At a later date, three or four weeks afterwards, a bilateral block dissection is carried out to remove the lymph nodes in both groins.

Cytological studies carried out on malignant melanoma in animals before and after irradiation

tion with high-voltage X-rays of various doses (figs. 6, 7 and 8), and on malignant melanoma in patients, have shown that, on the whole, this tumour is not radiosensitive. Thus, wherever possible, radical surgical excision must be carried out.

ACKNOWLEDGMENTS

I wish to thank my colleagues at the Royal Cancer Hospital—Mr. C. E. Shattock, for allowing me to publish Case III; and Mr. R. C. B. Ledlie, for Case II; and Dr. P. C. Koller, for help in the cytological studies.



FIG. 6.

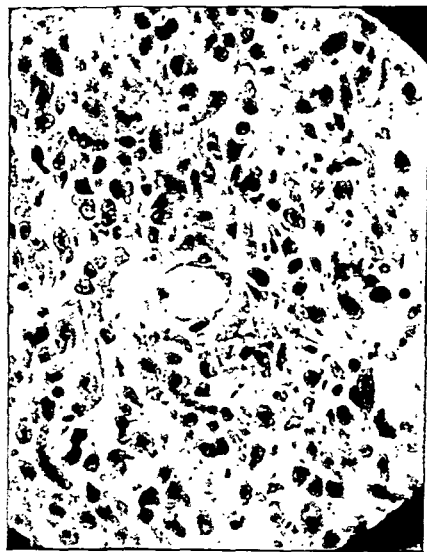


FIG. 7.

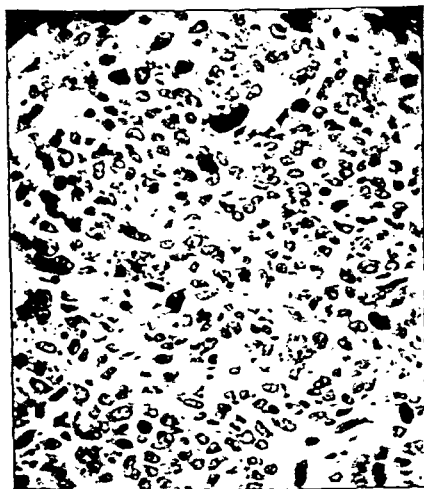


FIG. 8.

FIG. 6.—Cytological study of a biopsy specimen of a melanoma in a dog showing the histological variability of the tumour. The lower part of the section is rich in melanoblasts and chromatophores: the cells are long and spindle-shaped: some are large containing cytoplasm rich in pigment. The upper part contains round cells which are actively dividing: few pigmented cells are present ($\times 400$).

FIG. 7.—Cytological study of the same tumour shown in fig. 6, after X-irradiation with a total tumour dose of 2,500 r. No changes are present and actively dividing cells are shown ($\times 700$).

FIG. 8.—Cytological study of the same tumour shown in fig. 6, after X-irradiation with a total tumour dose of 3,500 r. No favourable irradiation reaction is present ($\times 400$).

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Spreading Ulceration of the Skin Associated with Idiopathic Ulcerative Colitis

By E. C. B. BUTLER, F.R.C.S.

PROGRESSIVE ulceration of the skin is a rare but important complication of ulcerative colitis. In America Jankelson and McClure (1940) reported 7 cases, citing 12 others from the literature and Felson (1941) described 3 cases. Jankelson and McClure thought the condition was due to a vitamin deficiency while Felson ascribed it to an impaired resistance to infection. No British reference has been found so far.

CASE I.—A married woman aged 30 was admitted on August 8, 1942, to the London Hospital with the following history: Her first attack of ulcerative colitis, proved by sigmoidoscopy, occurred in 1934. In 1938 she had a further attack lasting for some months. She had remained well until six weeks before admission. Since then she has suffered from severe diarrhoea and rectal bleeding.

On admission there were no unusual signs. The stools contained blood and pus. No pathogenic organisms were isolated.

1.9.42; She complained of a small raised painful swelling on the left shin. Five days later a blood transfusion was given in the left arm by cutting down on the vein. Soon after an ulcer formed at the transfusion site.

7.9.42; The swelling on the leg broke down to form an ulcer which spread very rapidly. Although the discharge from the ulcer was profuse and purulent, repeated cultures remained sterile for some days. After this secondary infection occurred. Many organisms were then cultured from the ulcer; *Staph. aureus* predominated.

The base of the ulcer was composed of pus and sloughs but the infective process did not go beyond the deep fascia. The edge was raised, red, exquisitely tender and undermined. The skin surrounding the ulcer was red and indurated to a breadth of $\frac{1}{2}$ in. Spread of infection occurred in a very characteristic manner. The raised undermined edge rapidly dissolved away into pus leaving a fresh red area which, in turn soon became undermined and necrotic.

A similar ulcer also formed on the left arm at the site of the first blood transfusion.

The pain was so intense that the patient screamed whenever the dressings were changed or the affected limbs moved.

Local therapy consisted of hypertonic saline dressings, local sulphonamides and ultraviolet light. General measures included repeated blood transfusions, oral sulphonamides and a low residue, high vitamin diet. In giving the transfusions care was taken not to cut down on a vein.

The ulcers continued to spread until by October 14 all the skin of the leg had been destroyed from just below the knee to the level of the ankle (fig. 1). A similar ulcer had involved two-thirds of the left forearm. The patient was critically ill.

On October 15 the red growing edge of both ulcers was completely excised with a diathermy knife. The skin and superficial fat only were involved. Pathological report showed pyogenic infection. The next day pain had disappeared. The edge of the ulcers remained clean and clear-cut: there was no circumferential reddening of the skin. The discharge appreciably diminished and soon fresh epithelium grew in from the periphery (figs. 2 and 3).

Local treatment consisted in the repeated application of sulphathiazole powder. Whereas before operation local chemotherapy seemed inefficient post-operative treatment was successful. Possibly the pre-operative failure was due to the excessive discharge which rapidly rendered the sulphonamide powder inactive.

On October 19 an enormous rectal hæmorrhage occurred; the pulse-rate rose to 158. Five pints of blood were given. After this relapse secondary infection of the muscles of the arm occurred. On December 12 the left arm was amputated: two more pints of blood were given during the operation. The wound healed perfectly, no further spread occurred in the leg. Rectal bleeding ceased. In February 1943 she went home, her weight was rising, the ulcer was clean, her bowels were open twice daily and contained no blood.

In October 1944 the leg was grafted by Mr. Rainsford Mowlem with an excellent result.

In October 1945 she was readmitted to the London Hospital for delivery of a full-term child. While in hospital the leg remained healed although there was some further diarrhoea and hæmorrhage from the rectum. No further ulceration has occurred up to the present.

CASE II.—A woman aged 40 was admitted on November 11, 1944, to an Emergency Hospital with bilateral painful ulceration of the legs. She stated that the ulcerative colitis began in 1939 and in 1941 she had had a transverse colectomy, followed by a terminal ileostomy in 1942. In 1943, Mr. Hermon Taylor performed a partial colectomy, the ascending and part of the transverse colon were not removed.

On admission her condition was good: she had irregular pyrexia, the discharge from her colon had increased lately and consisted of blood and pus. On both legs there were large ulcers with raised red tender undermined edges. The bases were composed of pus and sloughs. *B. proteus* and *Str. hemolyticus* were obtained from cultures at different times. The treatment consisted of a high-vitamin low-residue diet. Systemic penicillin 120,000 units daily was given for a week. Penicillin

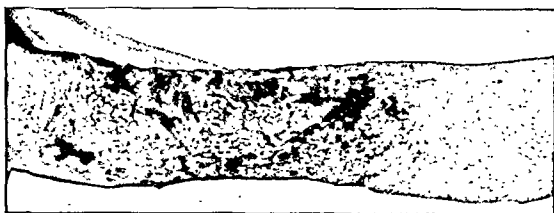


FIG. 1.—Left leg 1.10.42.



FIG. 2.—Left leg 2.11.42.

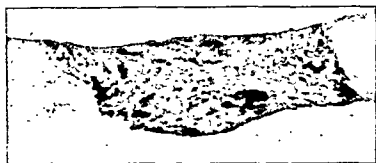


FIG. 3.—Left arm 2.11.42.

powder was applied locally. During this time her condition deteriorated and the ulcers doubled their size.

On December 3 the edge of both ulcers was excised with a diathermy knife, oozing was checked by elevating the legs during the operation. Another blood transfusion was given.

Post-operatively penicillin sulphonamide powder was applied locally. The remains of the colon was irrigated daily with a suspension of succinyl sulphathiazole.

The ulcers stopped spreading and the discharge from the colon practically ceased.

In January the patient was transferred to the care of Mr. Hermon Taylor. During the next month further discharge from the colon took place and the ulcers again became painful with renewed spread. In March Mr. Hermon Taylor excised the remainder of the colon.

Pathological report: Pyogenic infection of the colon with chronic inflammation of the lymphatic nodes.

After the operation the patient's general condition rapidly improved. The ulcers ceased to spread and gradually healed: skin grafts were not required.

In April 1945 she was sent home and has remained well since.

DISCUSSION

In both our cases the ulceration was severe but it is evident from the literature that all grades of skin involvement may occur in association with ulcerative colitis and we have met other mild cases where the ulcers were not painful and healing rapidly occurred with rest and chemotherapy. In this paper, however, we are chiefly concerned with the severe skin lesions since their clinical picture is so unmistakable and because they may be a danger to life.

Ætiology.—The ulceration seems to occur in patients who have suffered from colitis for some time; in both our cases and in others reported elsewhere the skin ulceration commenced during an exacerbation of the colitis as shown by pyrexia, diarrhoea and rectal bleeding.

We also noted that healing of the ulcers appeared to depend on the cessation of the active phase of the colitis, in one case following medical treatment and in the other after colectomy. It was noted in the second case that a relapse of the colitis was accompanied by an exacerbation of the skin ulceration.

These facts suggest that the skin lesions are clearly linked with the colitis but in what way is at present uncertain.

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incidence of the former being variously reported between 25% and 75% and of the latter between 20% and 97·8%. Secondary disease may also follow the bursting into the rectum of gonococcal abscesses, e.g. from the prostate, Cowper's glands or fallopian tubes. The high incidence of secondary involvement in the female is due to the close proximity of the anus to the vagina, infection being more likely to occur during defaecation and menstruation. In spite of the advent of the sulphonamides and penicillin, the incidence of secondary disease in women has not lessened and in a recent series Nicol reported it to be 35%.

Primary disease, occurring more frequently in males than females, follows sodomy but many accidental infections due to the insertion of contaminated thermometers or enema nozzles have been reported. Stühmer (1921) described infections in 26 soldiers which had followed prostatic massage with a glove contaminated with gonococcal pus.

I have treated females with both primary and secondary involvement but the following observations concern 168 cases of primary disease in the male, contracted by sodomy.

Signs and symptoms.—Anorectal gonorrhœa may have an acute or subacute onset. In my experience the acute phase of the disease is rarely observed (it was noted in only 4 of my series) and a large majority of patients with positive findings will give no previous history of any acute manifestations. Acute signs and symptoms more often occur during the subacute phase when they are due either to perianal and ischio-rectal abscess (often leading to fistula) or to fissuring of condylomata acuminata.

The 4 cases in my series with early acute signs and symptoms complained of severe burning pain and tenesmus with blood in the stools and defaecation was extremely painful. Proctoscopy revealed a generalized redness of the rectal mucosa with localized areas of large red infiltrations similar to those of gonococcal urethritis, which bled on the least trauma and bulged into the instrument. Superficial erosions were seen in 2 cases but never ulceration—a pathological curiosity in all gonococcal inflammations. A frankly purulent discharge (hæmorrhagic on two occasions) was seen between the infiltrations on the rectal mucosa. There was no obvious involvement of anal canal in spite of the fact that gonococcal pus was present at the anal orifice.

Subacute inflammation was present in the majority of my cases and in 64% the disease was symptomless, an examination being requested because of anal warts or because the sexual partners had contracted a gonococcal urethritis. 40 in my series had noticed mucus or mucopus (occasionally hæmorrhagic) on the stools. Those with symptoms complained of moisture or itching in the region of the anus and, as already mentioned, acute symptoms due to perianal or ischio-rectal abscess, fistula and occasionally fissuring due to condylomata acuminata, were observed. (Painful fissuring, in my experience, is much more frequent in association with primary and early secondary lesions of syphilis.) Proctoscopy in the subacute phase of the disease shows more changes in the anal canal than rectum. Patchy areas of redness or more conspicuous submucous infiltrations, red or pale in colour, are seen on and between the columns of Morgagni, being especially well marked at the anorectal junction. Submucous infiltrations, pale in colour, are also seen on the rectal mucosa and I have occasionally observed their surface to be granular. Small superficial indurated areas are occasionally palpated in rectum and anal canal. There is an excess of adherent mucus on the mucous membrane of both the rectum and anal canal and occasional streaks (rarely clumps) of mucopus.

Complications.—Gonococcal inflammations in the subepithelial connective tissue of rectum, anal canal and skin of anus may cause local areas of induration which may either resolve or suppurate to cause perianal or ischio-rectal abscess with or without the subsequent development of fistula. 8 of my cases, at the first visit, were suffering from fistula and 3 of these had undergone surgical treatment. Gonococci were demonstrated in the discharge and all cases responded to specific treatment; no cases developed abscesses or fistula during treatment. It is interesting to note that 6 of Stühmer's cases developed abscesses and in 1 gonococci were demonstrated in the discharge five months after incision.

Condylomata acuminata, due to a concomitant virus infection, are present more frequently in anorectal than in urogenital gonorrhœa which is possibly explained by the fact that the anal canal is more liable to trauma than the urethra. The lesions, situated on the skin of the anus or in the anal canal as far as the anorectal junction, occurred in 40 (24%) of my cases and were the most frequent complication.

Superficial fissuring was only observed in 3 cases, all in association with condylomata acuminata.

The only blood-borne complication was arthritis which occurred in 2 cases, 1 with a positive complement-fixation test on the blood serum and in all probability gonococcal, and the other with a negative blood test and no doubt due to pleuropneumonia-like organisms or a virus.

Pathology.—During the last ten years I have studied the minute pathology of gonorrhœa
JULY—PROCT. 2.

It is possible that several factors play a part. First there may be a deficiency due to a lack of biosynthesis of certain vitamins in the diseased bowel; secondly the original skin lesion may be an allergic phenomenon similar to that which originally may have caused the colitis. This view is supported by the fact that in one of our cases the discharge from the ulcer was sterile for several days which was against a diagnosis of primary bacterial infection.

Thirdly, lowered resistance of the patient to infection coupled with secondary anaemia undoubtedly promotes the incidence of the severe secondary infection which so often occurs in these cases.

Bacteriology.—In our first case cultures from the lesion were sterile for some days before pyogenic infection occurred. The second case was not admitted to hospital until secondary infection was well established. Cultures from our cases showed at various times staphylococci, haemolytic streptococci, *B. proteus* and *B. pyocyaneus*.

The lesion commences as a raised red papule which rapidly breaks down to form a small ulcer. In mild cases no further spread may occur but in others the discharge becomes profuse and the ulcer rapidly increases in size. Severe pain is a predominant feature. The commonest sites for infection to occur are the limbs but any part of the body may be affected.

Unless the condition is checked the ulcer may spread until the patient is in danger of dying from toxæmia and anaemia. Spontaneous arrest may take place if there is a clinical improvement in the colitis but in severe cases energetic local and general treatment is required to halt the spread of the ulceration.

Once the infective process has been healed epithelium rapidly grows in from the edge of the ulcer but skin grafts may be required when the lesion has been extensive.

Treatment.—Severe cases must be treated vigorously; our first patient nearly died because the diagnosis was not made early enough.

If the colitis is in an acute stage (Case I) medical treatment will probably suffice. Diet should have a high protein content, a low residue and plenty of essential vitamins. Oral sulphonamides and systemic penicillin should be given but in our two cases the results from chemotherapy were disappointing. It is possible that larger amounts of penicillin, say one million units daily, might have had a more favourable result. Repeated blood transfusions are essential to combat the secondary anaemia.

If the patient does not improve ileostomy should be considered. In more chronic cases (as in Case II) surgical treatment may be required more frequently since the skin lesions may relapse with each exacerbation of the colitis. Ileostomy may be required and colectomy is often advisable. Locally we found that the treatment which appeared to stop the spread of the ulceration was excision of the whole of the edge with a diathermy knife. The result was dramatic, pain vanished, the edge of the ulcer became clean and clear-cut and the response to local chemotherapy was good. At operation the limbs should be raised to avoid considerable blood loss from venous oozing. These patients do not tolerate loss of blood and every effort should be made to prevent undue hæmorrhage. Blood transfusion is advisable during the operation. Excision with an ordinary knife might be equally satisfactory but the diathermy appeared useful in preventing blood loss. Complete excision of the whole ulcer, including the base followed by immediate skin grafting may be successful; this was done on one facial ulcer by Mr. C. L. Heanley with excellent results.

Post-operative therapy consists in repeated application of penicillin sulphonamide powder with early skin grafting if necessary.

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Anorectal Gonorrhœa

By A. H. HARKNESS, M.R.C.S., L.R.C.P.

GOÑORRHŒA, syphilis and lymphogranuloma inguinale frequently involve the rectum and anal canal. Granuloma venereum and chancroid usually only cause lesions in skin of anus and skin of anal canal. I have seen also several cases of primary abacterial or Walsch urethritis (one subsequently developing Reiter's syndrome), contracted by sodomy, in which smears of the urethral discharge showed the presence of inclusions and cultures yielded pure growths of pleuropneumonia-like organisms. These organisms were isolated also in anal swabs of the only contact examined.

Anorectal gonorrhœa is a disease which is much more frequent than is generally supposed but owing to the mildness of its signs and symptoms it is often overlooked.

The disease may be primary or secondary. Secondary manifestations occur chiefly in women with primary urogenital involvement and in little girls with vulvo-vaginitis, the

Section of Anæsthetics

President—JOHN CHALLIS

[February 6, 1948]

Anæsthesia in Babies and Children

By R. W. COPE

DUBOIS and others have shown that from birth to puberty the metabolic rate is higher than at any other time during life, and is far higher than might be expected for the size of the organism. Running parallel with the curve of metabolic rate is that of oxygen demand and reflex irritability. Apprehension and fear are potent sources of raising the metabolic rate and it is by suitable premedication that the metabolic rate is reduced.

Premedication.—The value of bringing a child asleep to the operating theatre region is inestimable both to the child himself and to his parents. Let your own human feelings of sympathy for other people's fears be shown when you first approach a child about to have an anæsthetic. There are efficient methods now available to overcome those natural fears on the part of the patient, and briefly they are resolved into the following methods:

The rectal route.—*Paraldehyde:* The dose is $\frac{1}{4}$ to 1 drachm per 14 lb. (3 to 4 c.c. per 6.3 kilos) of body-weight in a 10% solution of normal saline, and should be given forty-five minutes pre-operatively. The sleep obtained after twenty minutes is very deep, and there is a marked diminution in the amount of anæsthetic drug which is necessary later. The post-operative sleep is quiet and will tide the child over the first few hours of pain arising from the surgical wound. Other methods of inducing pre-operative sleep are well known and will be only briefly mentioned:

By mouth: The oral barbiturates, such as nembutal or seconal.

By injection: The intravenous barbiturates, whose use may be limited only by the size of the patient's vein and his natural dislike of the prick of the needle from a strange doctor.

There is, however, one method of premedication by injection to which more attention might usefully be paid. This is by the administration of the opiates, morphia and scopolamine. Magill and Rowbotham, amongst many others, have described their effects. Bearing in mind the way in which morphia and hyoscine obtain sedation by a lowering of the body's metabolic rate, it can be appreciated how a child might respond particularly well to such a drug. The dose recommended has been calculated on a body-weight basis at morphia 1/30 grain per stone (2 mg. per 6.3 kilos) and scopolamine 1/1000 grain per stone (0.06 mg. per 6.3 kilos).

Induction and maintenance of anæsthesia.—Because the high metabolic rate has been lowered by premedication it is important to choose a method of anæsthesia which carries an adequate supply of oxygen. This fact has been recognized for many years but it is worth stressing lest there should become established some agent such as nitrous oxide which, if used without an adjuvant drug, may cause a dangerous degree of anoxia in the child.

It is true that nitrous oxide with minimal oxygen is employed in dental extraction clinics for children everywhere with great success, and yet I cannot help thinking that I am witnessing stages of asphyxia rather than anæsthesia when such a method is used. I believe the success of the method lies in the shortness of the operation.

Again during the start of an anæsthetic on an ill child he may change rapidly from a person who is breathing quietly and easily to one who has ceased to breathe, who passes quickly through the intense lividity due to respiratory obstruction to a flaccid, pale grey infant with dilated pupils, whose life is slipping quickly away. All these changes take place in a short space of time so that to the need for adequate oxygenation must be added the old-established fact of maintenance of a perfect airway.

For induction, therefore, it has seemed to us at Great Ormond Street that there is nothing safer than ethyl chloride or divinyl ether (vinesthene) sprayed on to an open or semi-open mask.

from biopsy material obtained by means of a punch (E. T. C. Milligan) from rectal mucosa, anal mucosa and skin of anal canal of 9 of my cases.

Rectum.—Several specimens show areas of disorganization and degeneration of the columnar mucus-secreting epithelium both on surface and in crypts of Lieberkühn and in some areas it is destroyed entirely with exposure of the subepithelial connective tissue. In the subepithelial connective tissue there is engorgement of capillaries which are surrounded by a cuff of polymorphs, lymphocytes, plasma cells and monocytes. Inflammatory cells are too numerous to show any evidence of exudate. Gonococci, chiefly extracellular in position, are seen in the necrosed mucous membrane. Intracellular organisms are seen more frequently in the subepithelial connective tissue and are particularly numerous beneath the necrosed mucous membrane. Their number diminishes as one approaches the muscularis mucosae and organisms were never seen in or beyond this structure.

Anal canal.—No changes are observed and no gonococci are seen in the stratified cuboid or modified squamous epithelium of anal canal, although the tissue reaction in the subepithelial connective tissue of the anal canal and the presence of gonococci both intra- and extra-cellular in position was similar to that seen in the rectum.

These investigations show that the portal of entry of gonococci in anorectal infections is the columnar epithelium of the rectum and that involvement of the subepithelial connective tissue of the anal canal is secondary. How high the infection travels by the subepithelial or surface route I do not know but Gant (1923) and Cress (1917) state that the inflammatory process extends upwards to involve the sigmoid and descending colon and the only evidence brought forward to support this is that of Cress who described a case "with tenderness on deep pressure over the left lower quadrant of the abdomen". Our opinion is that the infection never goes higher than the rectum but we hope to verify this by an examination of biopsy material from the sigmoid flexure of our next case.

Diagnosis.—Diagnosis depends on identifying gonococci by Gram's method in smears of the discharge or streaks of mucus. Smears, in my opinion, which is perhaps unorthodox, are superior to cultures in these cases as they are in urogenital infections. It is an easy matter, however, in certain cases, to obtain pure cultures of gonococci since the normal flora appear to be absent.

Proctoscopy is unnecessary for diagnosis in quite a large percentage of cases in which gonococcal pus is either present at the anal orifice or forced there by evertment, two or three times, the margins of the anus. Failure in diagnosis by this method demands proctoscopy and several slides are made of any suspicious secretions in rectum and anal canal. I have also had several cases in which a diagnosis was only made after an examination of mucus or pus on the stools.

The gonococcal complement-fixation test on the blood serum is, in my opinion, rarely helpful in diagnosis of primary anorectal disease as it was negative in 90% of my cases.

Differential diagnosis.—Granular proctitis is perhaps the only rectal lesion which may be confused clinically with gonorrhoeal proctitis. Both conditions cause a discharge but in granular proctitis the changes in the mucous membrane are much more marked in extent and intensity.

Treatment.—In all gonococcal infections I prescribe, in the first place, sulphonamide therapy (sulphathiazole or sulphadiazine 1 gramme six-hourly for five days) in view of the dangers of masking the development of a concomitantly acquired syphilis. Such a precaution is particularly important in the treatment of anorectal gonorrhoea as the rectum or anal canal is frequently the site of primary syphilis as is shown by the fact that in my series of 168 cases the Wassermann and Kahn reactions were positive in 60 (35%).

Penicillin, used only when the condition is sulphonamide-resistant, may be given parenterally (either one injection of 300,000 units in a delaying vehicle or five injections of 40,000 units two-hourly) or orally in tablets containing 20,000 units in 0.5 g. of disodium citrate (6 doses of 3 tablets three-hourly).

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The following papers were also read:

Factors Influencing Fatality in Abdomino-perineal Excision of the Rectum.—Mr. STANLEY O. AYLETT.

Abdomino-perineal Excision of the Rectum after Left Iliac Colostomy.—Mr. FRANK FORTY.

If the child appears cyanosed before induction starts, as for example in the case of a child with bronchopneumonia yet requiring an acute mastoid operation, then an open mask induction of ethyl chloride and ether followed by nitrous oxide, oxygen and ether will carry that child safely through the operation.

It is this use of ether, with its absence of post-operative complications, whether they be pulmonary or vomiting, which has kept this agent as the one most commonly used at Great Ormond Street.

Congenital hypertrophic stenosis and other congenital abdominal abnormalities needing laparotomy (for example exomphalos and duodenal atresia). At Great Ormond Street Rammstedt's operation is performed by one surgeon using local infiltration alone and he has used this method for many years. His mortality and morbidity results are first class. It is then found that three other surgeons, including the senior surgeon to the hospital point to a list of successful operations, equally long, performed under general anaesthesia. When general anaesthesia is used ether or divinyl ether or a mixture of the two using nitrous oxide and oxygen as its vehicle has been used. The same description applies equally to those other abdominal conditions requiring laparotomy. That of duodenal atresia must be mentioned again; it will be remembered that this operation must always be of long duration and necessitates the performance of a gastro-jejunostomy when the primary condition has been verified. These facts made me first realize that the baby's condition might be improved if the depth of the anaesthesia could be lightened during the course of the operation and then deepened rapidly without any outward sign from the patient. In such a young baby control of the airway by a pharyngeal airway was often unsatisfactory in my hands. Glottic spasm would occur rapidly if the depth of the anaesthesia at the moment of incising the peritoneum in the epigastrium was ill-judged, and having once occurred was more difficult to overcome than in an adult. For both these reasons I began to pass a No. 00 Magill tube under direct vision, in all these babies undergoing laparotomy, as soon as surgical anaesthesia was established.

The quiet respiration which is obtained throughout an abdominal operation in an adult

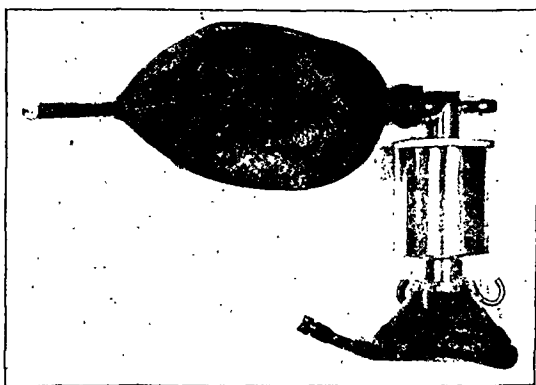


FIG. 1.

by this manoeuvre is well known, and the depth of anaesthesia can be safely lightened during the performance of an intestinal anastomosis. As might be expected the same type of respiration is apparent when intratracheal anaesthesia is used on a baby.

To assist further in producing a quiet respiration in babies undergoing abdominal surgery, a method of carbon-dioxide absorption has been tried recently which indicates further trial. A few well-known types of circle apparatus for carbon-dioxide absorption have not been entirely satisfactory, perhaps due to the increase of the dead space of the patient. Stimulated by a communication from Kaye of Melbourne, an attempt was made to build a light canister for soda lime of about the same capacity as the vital capacity of a baby. At 12 months this is found to be 150 to 200 c.c. The next step was to realize that the smallest size of baby's face mask was not designed to fit the baby's face accurately. In a baby there is underdevelopment of the chin compared with the adult chin, and yet a baby's facemask is nothing more than an exact copy of an adult mask on a reduced scale. Accordingly a mask was made by hand for me by Mr. Charles King, in which there is a slight lip to the lower margin of the mask, and this will now fit snugly on to the baby's face. Similarly the breathing bag has been reduced to the size of a BLB oxygen mask (see fig. 1).

The role of curare in abdominal surgery in children.—Though ether still remains the most common agent in producing relaxation in children there are still a few conditions in which perfect relaxation with a quiet respiratory movement is difficult to obtain. Splenectomy in children of 4 years and over is not uncommon and surgical manipulations could be better assisted if there was a very peaceful respiratory movement. To produce this result, in my last 4 cases tubarine in varying doses has been used. The difference in the appearance of the abdomen as the surgeon worked to deliver the spleen from under the costal margin was striking. Exomphalos is another rare condition in which very great relaxation is needed in order that the surgeon may close the abdominal wall, a procedure as difficult as closing the abdominal wall after having returned the contents of a large diaphragmatic hernia to the abdomen. In a recent case, aged 36 hours, the mass was almost the whole liver and many coils of intestine. The body-weight was 7 lb. 6 oz. An intravenous drip was in position. It should be remembered that a blood transfusion is often necessary due to tearing of the liver surface with consequent excess bleeding. After inducing anæsthesia with cyclopropane and oxygen, an intratracheal tube was passed and the baby's canister mask reapplied. 1-mg. of tubarine was then injected intravenously. Profound relaxation without complete paralysis was obtained throughout the operation, recovery was uneventful.

Harelip and cleft palate repair.—The age at which the first operation for the complete repair of a harelip is performed is from 2 months onwards. The keynote for success in these operations lies in producing a quiet operating field for the surgeon combined with safety for the baby, and the following points are of value: (1) The use of a wide-bore intratracheal tube. (2) Careful packing of the oropharynx, preventing blood from running down into the air passages or stomach. (3) Care taken to ensure that the baby has recovered all his reflexes by the end of the operation.

At Great Ormond Street, looking at the figures for deaths on the operating table before intubation was used as a routine for these operations, it was found that in 1924, 1925 and 1929 there were 5, 4 and 6 deaths in each year. On examining the causes of death we find that the harelip cases occur in the following order: 1, 1 and 2. After intubation became routine practice the total death figures for 1939 and 1945 drop to 1 and 2, and harelip conditions do not enter into any of these cases.

In 1920 Magill first began to pass an intratracheal tube on a baby. By reason of the very small size of tube necessary, a new anxiety has arisen for the anæsthetist. This is kinking and obstruction of the tube as it passes over the dorsum of the tongue. Two types of tube designed by Magill are used by us at Great Ormond Street to overcome this difficulty. One is an ordinary rubber tube strengthened by sliding over it a thin outer rubber tube and only the single or inner tube is passed through the vocal cords. The other is a Magill armoured tube consisting of a finely coiled spring covered with rubber, to whose proximal end is attached a double funnel opening. The anæsthetic vapour is directed to the fine tube, while the broad funnel end is left open to the air. This entry and exit for the anæsthetic gases achieve exactly the same purpose as Ayre's T-piece. My own preference is to use the armoured tube for all harelip and cleft-palate operations.

Intubation.—The chief factors which have given me trouble in passing a tube through the tiny opening of the larynx are: First, the opening into the mouth may be considerably obstructed by a round knob of tissue, the freely mobile premaxilla. In order to get this mobile proboscis out of the way Denis Browne designed a special blade for the Magill laryngoscope. The curved shelf of this blade is designed to keep the premaxilla out of the way of the groove down which the tube is to pass.

My own feeling is that this blade is too large for the mouth and it is my practice to use the Shadwell laryngoscope designed by Gillespie. In order to prevent the blade falling into the cleft, or the premaxilla obstructing the groove of the instrument, it has seemed easiest to insert the blade into the right-hand corner of the mouth and to keep it there throughout the manipulation while the cords are visualized.

The anatomy of the infantile larynx.—It will be remembered that in the newborn the distance from the gums to the glottis is 2 in. and the distance from the glottis to the bifurcation of the trachea is a further 2 in.

Epiglottis: There is a marked difference in contour between the infantile epiglottis and that of the adult. In the latter the epiglottis is a leaf-like structure, quite flat in the antero-posterior plane. In the infant this is not the case, the lateral margins of the epiglottis are rolled slightly on themselves towards the mid-line. This appearance will decrease the size of the visible epiglottis even more, and this fact should be recognized when the laryngoscope is used to lift the tip of the structure forward. Then will appear the tiny opening of the larynx through which the tube must be gently introduced.

After careful insertion of the gauze packing the baby requires very little ether to keep the cough reflex abolished and the body still. It should be your aim to lighten the anæsthetic so much that by the time the tube is removed there is a vigorous cough reflex and a good cry is produced before the baby leaves the theatre.

The removal of tonsils and adenoids by dissection is still the commonest operation performed in surgery, and for that reason it is pertinent to mention the method of anæsthesia used at the Hospital for Sick Children, Great Ormond Street. At that hospital neither the technique of the operation nor of the anæsthetic has changed greatly since 1907. In that year Waugh began to dissect the tonsils and curette the adenoids under deep chloroform, administered through a Junker's inhaler. Later a change was made to deep ether, using air from a foot-bellows, or oxygen as its vehicle. The vapour is delivered to the patient's mouth by a hooked metal tube, whose design has not changed since Waugh first described the operation. The airway is maintained by placing a sandbag beneath the shoulders, opening the mouth with Waugh's gag and then the tongue is drawn firmly out of the mouth by a pair of tongue forceps held by a nurse. Throughout the operation the surgeon wishes to have the patient at a deep plane of anæsthesia with no sign at all of movement of the palate or fauces, and this level is maintained while the adenoids are removed at the end of the operation. The child is returned to bed in the semi-prone position with the tongue forceps still in place, and these are removed when the cough reflex is brisk.

Anæsthesia for major thoracic surgery.—The scope of this surgery has increased rapidly in special units and I claim no recent personal experience of this work. My colleague, B. G. B. Lucas of Great Ormond Street and University College Hospital has kindly shown me his methods. He employs the same principles of physiology and anæsthesia in children undergoing pneumonectomy or lobectomy as he would use in adults. The use of intra-bronchial suction and of carbon-dioxide absorption with controlled respiration when required, sum up the technical procedures carried out.

THE ROLE OF ANÆSTHESIA IN THE STUDY OF AUTONOMIC NERVOUS SYSTEM IMBALANCE

A few words on this subject should be included here, for it has seemed to me that anæsthetists may assist and carry out useful research in at least two major surgical conditions of children.

(1) *Congenital megacolon (Hirschsprung's disease).*—It will be remembered that the large bowel receives its motor fibres from the parasympathetic system through the right and left vagus nerves and the second, third and fourth sacral roots. The sympathetic system supplies the inhibitory fibres which are given off from the spinal cord in the anterior roots of the fifth dorsal to the third lumbar segment.

In 1912 in the *Guy's Hospital Reports* Sir Arthur Hurst began to describe a theory of imbalance between these two nervous systems as the causation of this disease. In 1939 Telford first used spinal analgesia as a possible method of cure; the explanation of this treatment lay in the fact that by giving a spinal anæsthetic injection the whole of the sympathetic supply of the colon could be paralysed, so allowing the parasympathetic to supply an uninhibited field of action. Such an injection must, of course, reach as high as the fourth dorsal segment. It is found in many cases that there is a spontaneous bowel action soon after injection and it might be thought that the colon would relapse as soon as the paralysing action of the drug has passed. But such is not the case, for normal bowel-control sometimes remains for months after the initial spinal injection.

Telford's work has been repeated and I am familiar with the work of Hawksley at Great Ormond Street. In 1944 she described 12 personal cases in detail and her results were encouraging.

(2) *Congenital hydro-ureter.*—It has been thought that paralysis of the sympathetic system may assist these massive ureters and kidney pelves to contract so that there have been attempts at injection of the splanchnic ganglia with local anæsthetic solution. Scholefield and Chivers reported 5 such cases and their results have warranted further trial. It has, however, seemed to me that paralysis of the splanchnic ganglia is obtained more accurately by injecting the drug into the theca rather than attempting to inject it into and around the ganglia themselves.

Hawksley and I have used nupercaine 1/1500 as the spinal anæsthetic drug. The dosage has been determined by Howard Jones' method of measurement of the spine. Having determined the dose it has been my practice to make the injection in the third to fourth

lumbar space with the child sitting up, and from the moment of starting the intrathecal injection the patient is held vertical for the next fifty seconds. After this time a change is made to a 15 degrees Trendelenburg tilt and this is maintained for the next fifteen minutes. During this time the child is carefully examined for the height of skin anæsthesia developing, if this does not reach at least as high as the nipple line, it is reasonable to suppose that the sympathetic supply of the colon has not been completely paralysed. The injection should then be repeated in 48 hours' time.

This brings to an end the description of some points of anæsthesia you may find applicable in your own practice. For my own part I would especially like to thank my colleagues at the Hospital for Sick Children, Great Ormond Street, both Surgical and Anæsthetic, those who have gone before and those who in their varying capacities still labour there. All have taught me some of that quality of kindness in approaching that most important person in the operating theatre, the little child.

Dr. T. Cecil Gray considered that Dr. Cope was right in his advocacy of intubation. Even in tiny infants this undoubtedly conduces to a smoother and more trouble-free anæsthesia. Provided it was performed with extreme gentleness and with great care in the adequate sterilization of laryngoscopes and tubes it was not followed by harmful results. It appeared that in the type of closed circuit apparatus for children which Dr. Cope had described the soda-lime canister was situated directly above the facepiece and there might be a danger of inhalation of irritant dust. Dr. Gray asked whether Dr. Cope took any special precautions to ensure that this did not occur. In his experience children tolerated curare well provided one adhered to a dose for weight scale—2 mg. per stone (0.3 mg. per kg. body-weight).

Dr. Rex Binning admitted the advantages of employing parenteral premedication in children but stressed the need for some rule of thumb premedication for the routine tonsil list when it was often impossible for the anæsthetist to see each patient beforehand. He himself used seconal but post-operative restlessness was sometimes troublesome.

Dr. B. Kenton said that on the question of intubation each case had to be decided on its merits depending on the type of operation, the state of the child, &c. One had to remember, however, that the tidal volume in children was sometimes smaller than the sum total of physiological plus mechanical dead space. With intubation therefore the dead space is considerably decreased and thus tidal exchange facilitated.

Ayre's method was not mentioned though it was of great assistance in preventing CO₂ accumulation and obviating resistance to respiratory efforts. It would be interesting to know how it compared with Dr. Cope's CO₂ absorber.

Dr. Kenton drew attention to the use of seconal as a basal narcotic or the principal anæsthetic agent for minor surgery in children as advocated by Poe and Karp in America (*Current Researches in Anæsthesia and Analgesia*, 1946, 25, 152). The authors used doses of seconal of 0.1 to 0.14 grain per pound (6 mg. to 8.5 mg. per half kilo) of body-weight (with a maximum of 6 grains) given orally or rectally (in 5 c.c. of tap water) thirty to sixty minutes before the operation. Dose was decreased in anæmic and lethargic children. Nitrous oxide and oxygen in equal parts was used as a supplementary agent. The method was found useful by the speaker for such procedures as encephalography and ventriculography in children.

Dr. R. E. Pleasance stated that he had hoped to hear Dr. Cope's views on anæsthesia for the operation for strabismus in children.

Personally he had made use of small doses of curare, 5 mg. or less, and light anæsthesia. Relaxation of the eye muscles was almost immediate, and added materially to the ease with which the operation could be performed. Furthermore, the effect of the curare on the eye muscles lasted for some time after this had worn off in other parts of the body, thus allowing the traumatized muscles a valuable period of rest.

Small doses were essential, otherwise the muscles became too relaxed, and the surgeon complained that the eye felt like a ball of cotton-wool.

Dr. O. P. Dinnick found nembutal and seconal to be unreliable premedicants chiefly because digestion of the capsule is frequently inhibited—presumably owing to the child's anxiety. Splitting the capsule and disguising the taste with jam or honey gave better results, but he had largely abandoned these drugs in favour of sodium thiopentone administered rectally. The ordinary 5% solution was used and presented several advantages over other drugs administered rectally, namely, small bulk of solution, ease of preparation. A test for decomposition was unnecessary, and the drug was inoffensive. The dose was 1 gramme per 50 lb. body-weight (23 kilos)—slightly less in wasted or over-fat children—and was given an hour before operation using a record syringe and a very fine catheter inserted as high in the rectum as was comfortably possible. A preliminary bowel washout was not essential as it was found that with a very slow rate of injection the small amount of solution used seldom acted as an enema, especially if the buttocks were approximated with a strip of elastoplast.

He would like to stress that in infants the possibility of post-operative hyperpyrexia was a very

After careful insertion of the gauze packing the baby requires very little ether to keep the cough reflex abolished and the body still. It should be your aim to lighten the anaesthetic so much that by the time the tube is removed there is a vigorous cough reflex and a good cry is produced before the baby leaves the theatre.

The removal of tonsils and adenoids by dissection is still the commonest operation performed in surgery, and for that reason it is pertinent to mention the method of anaesthesia used at the Hospital for Sick Children, Great Ormond Street. At that hospital neither the technique of the operation nor of the anaesthetic has changed greatly since 1907. In that year Waugh began to dissect the tonsils and curette the adenoids under deep chloroform, administered through a Junker's inhaler. Later a change was made to deep ether, using air from a foot-bellows, or oxygen as its vehicle. The vapour is delivered to the patient's mouth by a hooked metal tube, whose design has not changed since Waugh first described the operation. The airway is maintained by placing a sandbag beneath the shoulders, opening the mouth with Waugh's gag and then the tongue is drawn firmly out of the mouth by a pair of tongue forceps held by a nurse. Throughout the operation the surgeon wishes to have the patient at a deep plane of anaesthesia with no sign at all of movement of the palate or fauces, and this level is maintained while the adenoids are removed at the end of the operation. The child is returned to bed in the semi-prone position with the tongue forceps still in place, and these are removed when the cough reflex is brisk.

Anaesthesia for major thoracic surgery.—The scope of this surgery has increased rapidly in special units and I claim no recent personal experience of this work. My colleague, B. G. B. Lucas of Great Ormond Street and University College Hospital has kindly shown me his methods. He employs the same principles of physiology and anaesthesia in children undergoing pneumonectomy or lobectomy as he would use in adults. The use of intra-bronchial suction and of carbon-dioxide absorption with controlled respiration when required, sum up the technical procedures carried out.

THE ROLE OF ANAESTHESIA IN THE STUDY OF AUTONOMIC NERVOUS SYSTEM IMBALANCE

A few words on this subject should be included here, for it has seemed to me that anaesthetists may assist and carry out useful research in at least two major surgical conditions of children.

(1) *Congenital megacolon (Hirschsprung's disease).*—It will be remembered that the large bowel receives its motor fibres from the parasympathetic system through the right and left vagus nerves and the second, third and fourth sacral roots. The sympathetic system supplies the inhibitory fibres which are given off from the spinal cord in the anterior roots of the fifth dorsal to the third lumbar segment.

In 1912 in the *Guy's Hospital Reports* Sir Arthur Hurst began to describe a theory of imbalance between these two nervous systems as the causation of this disease. In 1939 Telford first used spinal analgesia as a possible method of cure; the explanation of this sympathetic supply of the colon could be paralysed, so allowing the parasympathetic to supply an uninhibited field of action. Such an injection must, of course, reach as high as the fourth dorsal segment. It is found in many cases that there is a spontaneous bowel action soon after injection and it might be thought that the colon would relapse as soon as the paralysing action of the drug has passed. But such is not the case, for normal bowel-control sometimes remains for months after the initial spinal injection.

Telford's work has been repeated and I am familiar with the work of Hawksley at Great Ormond Street. In 1944 she described 12 personal cases in detail and her results were encouraging.

(2) *Congenital hydro-ureter.*—It has been thought that paralysis of the sympathetic system may assist these massive ureters and kidney pelves to contract so that there have been attempts at injection of the splanchnic ganglia with local anaesthetic solution. Scholefield and Chivers reported 5 such cases and their results have warranted further trial. It has, however, seemed to me that paralysis of the splanchnic ganglia is obtained more accurately by injecting the drug into the theca rather than attempting to inject it into and around the ganglia themselves.

Hawksley and I have used nupercaine 1/1500 as the spinal anaesthetic drug. The dosage has been determined by Howard Jones' method of measurement of the spine. Having determined the dose it has been my practice to make the injection in the third to fourth

Section of Odontology

President—HUMPHREY HUMPHREYS, O.B.E., M.C., M.B., F.D.S.

[March 22, 1948]

Unilateral Bony Swelling of the Maxilla

By Professor R. W. SCARFF, M.B., and D. GREER WALKER, M.B., M.Dent.Sc., F.D.S.

THIS paper presents some facts concerning a unilateral, bony swelling of the maxilla (figs. 1, a, b, c).



(a)



(b)



(c)

FIG. 1.

Different investigators have considered the lesion to be (I) a local or focal osteitis fibrosa; (II) a neoplasm; or (III) a hyperplasia.

(I) Knaggs (1926), who favours the diagnosis of osteitis fibrosa, says that: (a) The disease commences during childhood or during the growing period, and if left to itself may last a lifetime. (b) There is reason to believe it may become stationary or even go on to a spontaneous cure. (c) There is a complete absence of any periosteal bony deposit. (d) The affected bone is enlarged giving the impression of a swollen bone. "The resemblance to the normal bone remains, but the salient points that give the latter its 'expression' disappear." Davis (1941) differentiated between focal osteitis fibrosa and a tumour as follows: In focal osteitis "the enlargement is confined to the outer surface of the alveolus and its inner surface shows no swelling. On the other hand, a tumour expands the whole alveolus, forming more or less a globular tumour in the palate. This distribution of the swelling is a distinguishing feature between a tumour and osteitis".

(II) That this bony lesion of the maxilla is a neoplastic process can be concluded from the work of Thoma (1944), Phemister and Grimson (1937), and Furedi (1935). The term osteofibroma seems to be generally accepted. Phemister and Grimson in describing 13 cases of fibrous osteoma of the jaws (4 in the maxilla, 8 in the mandible, and 1 in both bones) say that, in general, the tumours are slow-growing, and when starting in childhood tend to become stationary in adult life. No case has been

real danger, and he would warn against the excessive use of mackintoshes and towels on the operating table, and a surfeit of wrapping and clothes post-operatively.

It was a common practice with adults to spray the larynx with local anæsthetic to facilitate endotracheal anæsthesia. He had found this technique of equal value for children and the cleft palate infants.

Dr. Cope had rightly stressed the difficulty of intubating infants with cleft palates. Dr. Dinnick suggested that if twenty minutes have been spent in two or three vain attempts at intubation, it is wise policy, incurring no loss of prestige, to cancel the operation for that day.

In his experience infants in the first forty-eight hours of life withstand operation and anæsthesia surprisingly well—it is in the ensuing few weeks until their birth-weight is regained that they are such poor risks. He would like to know if the greater experience of Dr. Cope confirmed this view.

He would hesitate to criticize Dr. Cope's CO₂ absorption technique without having seen it used, but felt there must be—as in all absorbers—a certain resistance to respiration and a significant amount of "dead space". His own experience was that infants tire quickly if they have to breathe against even the slightest obstruction, or were allowed to build up CO₂ under the mask. He therefore avoided the use of a facepiece as much as possible, preferring to maintain anæsthesia by oral insufflation or an Ayre's "T" piece if an endotracheal tube were used.

Dr. A. H. Galley said that it was a continual source of wonderment to him that babies and small children so often maintained an adequate airway when no pharyngeal airway was used at all; the supporting finger must not, however, migrate from the region of the symphysis mentis as pressure on the soft tissues of the submental region readily obliterated the airway. When administering spinal analgesia to babies (for therapeutic reasons) he had discarded lumbar-puncture needles. He mounted a needle as for venepuncture, advanced until he felt the needle-tip pierce the ligamentum flavum, withdrew the plunger to verify that the needle was well in the subarachnoid space and then made the injection.

Dr. H. Bruce Wilson said that he was pleased to hear that Dr. Cope underlined the prime importance of the maintenance of a clear airway during anæsthesia in children, and the necessity for adequate sedative premedication. He agreed that if a good airway could be maintained without intubation, that was to the good, but if difficulty were encountered he had no hesitation in intubating children of any age. The question of premedication had been exercising the attention of himself and his assistants at the Royal Aberdeen Hospital for Sick Children, and they had employed nembutal, rectal pentothal, paraldehyde, omnopon and scopolamine in an endeavour to determine which was most satisfactory. They had much satisfaction from oral nembutal and their success with this, compared with the experience of some of the other speakers in the Discussion, was perhaps due to the fact that they gave a small dose of nembutal the night before operation in addition to the dose before operation—probably the first dose had some "hangover" effect and made more certain of the action of the second dose. The drawback to nembutal was the period of restlessness and excitement during recovery. For this reason they had tried rectal pentothal and, being a shorter acting and more rapidly excreted drug, they found the period of post-operative restlessness very much more transient. The drawback to rectal pentothal was the need for close supervision and for a competent nursing staff.

Dr. J. D. Laycock asked if Dr. Cope could tell him how to give an anæsthetic to a child for a lipiodol bronchogram with due regard to explosive risks.

Dr. R. W. Cope in reply said: Dust from the close proximity of the small canister to the face mask was a real danger recognized at the start of its use. The speaker's own baby was induced to breathe into the new canister-mask in the early stages of experiment, and it was found that the baby's nose, lips and tongue were soon covered with a fine layer of lime dust. This dust formation had been prevented by taking care to add about 2 teaspoonfuls of water to the soda lime immediately before use. No further precautions had been necessary.

Ayre's method and the speaker's canister had not been compared either clinically or experimentally for an evaluation of the alveolar carbon-dioxide accumulation.

The suggestion of using small doses of curare to paralyse the eye muscles during operations for strabismus would seem to be valuable and the speaker was grateful for being told about the idea and the possibility of making the eyeball like cotton-wool would be borne in mind.

With regard to general anæsthesia for lipiodol bronchograms conducted in the X-ray department, there had been several techniques tried at Great Ormond Street. For some months the Anæsthetic Registrar had found the following method entirely satisfactory. Induction and maintenance were carried out with gas, oxygen and trilene. A Magill intratracheal catheter was passed through the mouth, and then the dose of lipiodol was introduced with syringe and record needle by injection through the wall of the tracheal tube. Anæsthesia could be maintained without anxiety during this manœuvre and while the pictures in different positions were being taken.

The cases seen early in life presented extremely healthy mouths as might well be expected. Those seen later had had teeth removed at various stages, on account of simple caries, and not for any gross infection. One case, aged 27, dates the swelling since the age of 7; at the age of 17 all his teeth were removed except an upper third molar (which presumably was unerupted) on account of caries.

The last clinical observation is the natural arrest of the condition. It is agreed that these lesions are arrested when the growth of the maxilla is complete. This is borne out by clinical evidence and is an important matter as far as treatment is concerned. We have not been able to follow these cases over a sufficiently long time to ascertain if they enter the realm of Paget's or leontiasis conditions as suggested by some authorities. Our view is in common with that of others who do not regard the lesion as belonging to either of these conditions.

X-ray examination is of the greatest value in the diagnosis of these conditions. It must, however, be stated that apart from X-ray and histological examinations no other special investigation revealed any data of value.

Histology.—In this group of swellings of the maxilla, histologically one must consider three different conditions:

A. True tumour: Rarely there occurs a true tumour in this region which appears to be locally invasive. This has been described by one of us (R. W. S.) previously. Its true nature is not yet determined, and for the present it must remain anonymous. This condition shows a characteristic histology: a cellular spindle-cell stroma, the cells of which are arranged around areas of calcification and areas of bone formation. It is possible that this condition is an atypical form of cementoma, but its behaviour is somewhat different. Although encapsulated in the early stages, if left alone it will invade and destroy the bones. The tumour appears to be radio-sensitive.

B. A lesion of the bone akin to, if not identical with, Paget's disease: There were 2 such cases in our series and fig. 2a shows the typical appearances, i.e. irregular bone formation, marked osteoclastic activity and a loose connective tissue stroma. This condition, too, would appear to be progressive.

C. Osteofibrous enlargements: This group contains 7 of our 9 cases. Although this lesion would appear to constitute an entity its nature is still in doubt. Histologically the condition shows fibrous tissue which varies considerably in cellularity in different cases and in different portions of the tissue from the same case. The bone present varies in amount and much of it is fully-formed lamellar bone with a trabecular arrangement. Fig. 2b shows a low-power view of such a case and gives some idea of the variation in cellularity of the fibrous tissue. Figs. 2c, d, are high-power views showing the great variation, and it will be noted that the bone is fully-formed lamellar bone.

The nature of these masses is in considerable doubt. They have been described by various authors as: chronic osteitis, localized osteitis fibrosa, Paget's disease, osteofibromata and hyperplasia. Chronic osteitis is not supported by the histology as the lesion shows no evidence of inflammatory infiltration. Even if one admits that localized osteitis fibrosa (Knaggs) is a positive entity the appearances of these masses do not correspond with this condition.

They show little osteoclastic activity; cyst formation is uncommon and much of the bone that is laid down is fully formed lamellar bone. The same is true of Paget's disease; the typical cases show none of the features of this disease. But in contradistinction to true tumours they are not localized and they become static after a certain stage of growth has been reached. Many workers have stated that there is frequently a history of trauma but that has not been our experience. We should prefer to regard the condition as a developmental hyperplasia possibly associated with trauma and analogous to osteochondritis juvenilis of the cartilage bones.

recorded which has become malignant. Blood calcium and phosphorus were determined in 4 cases and found to be normal. The lesion appears to be a true neoplasm and not a form of osteitis fibrosa, hyperostosis or chronic inflammation.

Thoma makes the following comments on fibro-osteoma: "This benign osteogenic tumour heretofore has been described under the name of localized osteitis, osteofibroma, ossifying fibroma, fibrous osteoma, or osteoid osteoma. The reason for all these names is easily understood when we consider the varied appearance and the changeable proportion of soft and hard tissue . . . I feel now that the terms localized osteitis fibrosa and osteodystrophia fibrosa are not in keeping with the pathological condition found. In the first place there is no evidence of osteitis as seen in Paget's disease, and second, the term fails to designate that the disease is an expansive new formation."

(III) It is perhaps a little unfortunate that most authorities have grouped this so-called tumour with similar though not identical lesions occurring in the mandible. This no doubt accounts for the multiplicity of terms. Furedi has stated that the maxillary tumour is somewhat of a different nature; and in speaking of osteofibromata of the maxilla questions whether they are true tumours or hyperplasias of probable inflammatory origin. In 1913 Westmacott reviewed 8 cases under the title "Chronic Hyperplasia of the Superior Maxilla". The ages of the patients ranged from 17 to 30 and he noted the following details: (1) The swelling is limited anteriorly by the premaxilla; (2) the alveolus is first affected and then the outer wall of the maxilla towards the malar process.

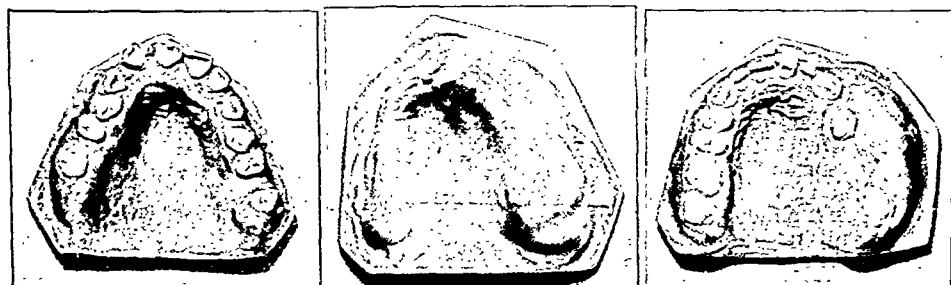
This brief review of the literature reveals the confusion that exists in describing these conditions. In this paper we make the following observations on 9 cases:

Age, sex and incidence.—The condition would definitely appear to begin in childhood. 5 cases were seen in patients under 20 years of age when the lesion had attained a considerable size; 3 under 30 years of age and 1 case aged 52. 5 of the cases occurred in female patients. It is extremely difficult to assess the degree of incidence. In reviewing several hundred cases of tumours our total of 9 cases over some ten years is low. There is no evidence of any hereditary tendency.

History.—No history of trauma could be obtained. This particular lesion is symptomless; many of the cases present themselves solely for cosmetic reasons or because in early life the parents notice the swelling, or when the swelling interferes with the making of a denture.

Examination.—The condition presents a definite clinical entity. The lesion appears to begin in the buccal aspect of the upper alveolus opposite the first molar and second premolar tooth—it extends in an upward direction involving the outer antral wall. This wall appears to become thickened and posteriorly the tuberosity is also involved. There is no anterior spread beyond the canine tooth. Later the extension occurs palatally but before this is discernible the "bending" of the medial raphe can be noted with its maximum concavity opposite the site of origin. The anterior part of the mid-line is not altered as in the more extensive bony lesions involving other facial bones. There is no encroachment on the nasal passage, fronto-malar synchondrosis, or zygomatic arch. The zygomatic bone shows involvement in the more extensive lesions as also does the anterior part of the floor of the orbit which may be slightly raised. On the affected side the eye will appear to be on a slightly higher plane but there is no disturbance of vision; the buccal mucosa is normal. The swelling is bony, hard, and painless; it is not well defined, and the bone rather gives the appearance of a "swollen bone". In only 1 case was the occlusal plane of the teeth affected. In this the maxillary teeth were displaced palatally and downwards. No alteration in size and shape of the teeth was noted, but slight spacing of the teeth has been noticed in the larger swellings, and the teeth themselves showed little evidence of infection.

case with Paget's disease. The lesions as they affect the palate and teeth have markedly distinguishing features as can be seen in figs. 3a, b, c. Of the more localized lesions producing a swelling of the maxilla we must consider soft tissue, dental and bony lesions. Soft tissue tumours (as for example carcinoma or mixed parotid tumours involving the antrum in whole or part) are easily differentiated from these bony lesions. Radiographs will exclude all soft tissue tumours and most tumours of dental tissues. The large odontomes are composed of calcified dental tissues. The appearance of these again shows characteristics which differ from the condition we have under consideration. The last group we have to exclude comprises the true osteomata, a tumour described by one of us previously (Scarff, 1947), and perhaps some early pagetoid cases. The true osteoma is more of an encapsulated tumour with all its inherent characteristics. It does not conform with the shape of the maxillary bone tending to lessen its marks of "expression". The tumour described by R. W. S. can also be excluded with the clinical difference that it is more localized in the early



(a) Leontiasis ossea.

(b) Paget's disease.

(c) Osteofibrosis.

FIG. 3.

stages with a later tendency to invasion, and to recurrence following removal. Some of the early cases of Paget's disease seen by us have shown alveolar changes which are distinct. These have been described by Sir Frank Colyer. One case, however, showed some swelling of the malar bone but again, we repeat, no other pathology conforms with the anatomical arrangement we have outlined. The recognition of this lesion as a definite clinical picture is borne out by the history, examination, and special investigations.

Treatment.—The treatment is usually conservative. There is no need for radical surgery in view of the nature of the lesion. Its correction for cosmetic reasons is justifiable; again, the making of a denture may necessitate some correction of the deformity. In either case a surgical trimming is all that is necessary.

We are indebted to Professor Kilner, Messrs. R. Vaughan Hudson, E. W. Peet, and J. W. Schofield for permission to include some of their cases, and to the radiologists of the Middlesex Hospital, particularly Dr. Campbell Golding, for their interest and help.

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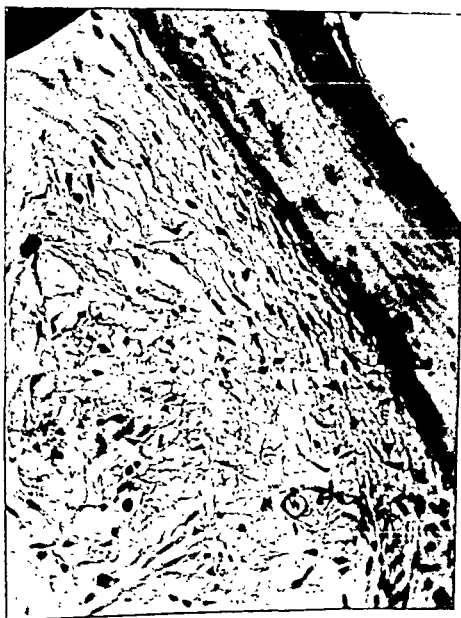
In the present state of our knowledge concerning these masses we have adopted the non-committal term—*osteofibrosis of the maxilla*.



(a) $\times 52$.



(b) $\times 52$.



(c) $\times 280$.



(d) $\times 280$.

FIG. 2.

Differential diagnosis.—We have already outlined the anatomical position and this excludes the leontiasis ossea group, which is not confined to the maxilla alone as is the

or of the face alone in which the condition of the teeth was not reported or in which accelerated eruption but not tooth-enlargement was noted, and a few others in which the teeth appeared normal at the time of examination.

CASES OF UNILATERAL HYPERPLASIA OF THE FACE IN WHICH TOOTH-ENLARGEMENT WAS REPORTED

There appears to be no record of such a case before 1863. In that year Friedrich published under the title "Unilateral congenital head-hypertrophy" the description of a girl of 16 in whom there was some unilateral enlargement, present from birth, of the face below the eyes, including chin, cheek, lips, tongue, tonsil and ear. He noticed pigmentation and more hair on the enlarged cheek, and found no difference in the bones except inside the mouth, where the alveolar processes on that side were much wider. Of the teeth he said: "The teeth of the right upper jaw, in particular degree the canine and the cheek-teeth, are much thicker, longer, and broader than on the left side . . . also in the lower jaw the teeth are more strongly developed than on the left." He observed that the teeth on the large side encroached across the apparent mid-line and that the gum was hyperplastic in both jaws on that side. Friedrich appended notes of another case which Heumann had seen seven years before but had not made known. This was a boy of 5 years in whom, since birth, there had been one-sided enlargement of the cheek, both jaws, and tongue. The teeth on that side were described as double the size of the others and wider apart, and the parents had noticed that the first teeth had erupted several weeks earlier on the large side than on the smaller.

There is a little uncertainty to what extent the findings as regards tooth-enlargement in this and some other cases are valid, for the following reason. It will be shown later that the eruption of the permanent teeth is sometimes so precocious on the enlarged side that by the age of 5 years the permanent teeth may be seen in the mouth on that side while the deciduous teeth are still in place on the other. To an observer who expected to find enlargement it might not be apparent that the difference in size on the two sides was due to this cause.

Passauer (1866) (fig. 1) found the size of the left cheek and the left side of the lips and tongue greatly enlarged in a boy of 11 years, and the teeth on the same side larger and spaced further apart. The left alveolar processes of the jaws were also wider. The mention by this author that the upper canine tooth was not only much larger on the left but was of



FIG. 1.—Passauer's case.

FIG. 2.—Barwell's case.

FIG. 3.—Cast of skull of Barwell's case.

FIG. 4.—Cast of mandible of Barwell's case.

abnormal shape is strong evidence in favour of his view that the tooth was enlarged, though the permanent canine on the other side may well have been still unerupted.

The next case was recorded by Barwell (1881) (fig. 2), a boy of 7 years. His reference to the teeth was ambiguous: "The baby teeth (on the left) form a strange contrast with the great incisors and molars on the right." However, the boy died of secondary hæmorrhage following an operation for ligation of the common carotid artery, and his skull was preserved in the museum of Charing Cross Hospital until about 1923. Keith (1923) studied it before its disappearance and had casts made which unfortunately were destroyed by bombs in 1941 (figs. 3 and 4). It was perhaps the only skull in which the condition could be studied, and Keith considered the bony development on the large side closely to resemble that found in acromegaly.

Examination of the few drawings and photographs remaining in the possession of Sir Arthur Keith which he kindly placed at my disposal enabled me to form an opinion as to

[April 9, 1948]

JOINT MEETING WITH THE SECTION OF ODONTOLOGY OF THE BIRMINGHAM
MEDICAL INSTITUTE, AT BIRMINGHAM

A Dental Abnormality of Size and Rate

By MARTIN A. RUSHTON, M.D., F.D.S.

THE size of the teeth and the rate of their development and eruption are matters of considerable importance in dental practice and attributes which we should often like to alter. Unfortunately they are characters very insusceptible to any influences which we may exert, and this applies particularly to tooth size. It is of some interest, therefore, to study a condition in which a striking abnormality of tooth size occurs, accompanied by an abnormality in the rate of development and by certain related disorders in the neighbouring tissues. Let us consider a moment what are the factors which are able to influence the size of teeth. There are genetic factors connected with family and race. Then in the direction of smallness we have the effects of radium and X-rays, certain genetic disorders affecting the mesodermal part of the tooth as in osteogenesis imperfecta and hereditary opalescent dentine, and perhaps some local inflammatory disorders such as osteomyelitis. In addition, in some forms of pituitary dwarfism of early onset the teeth may be on the small side of normal. In the direction of largeness the only suggestion of any factor other than genetic comes from the experimental work of Putnam, Teel and Benedict (1929) in which an alkaline extract of anterior pituitary gland was injected into 11-weeks-old puppies. The teeth were said to be larger than in the control and though unfortunately no measurements were published some of them certainly appear so in the illustrations. Downs (1930) in a similar experiment in which only slightly older puppies were used found no enlargement on measurement although other expected effects were obtained.

As regards rate of development of the teeth and rate of eruption we know of more factors. Clinically it appears that these rates can be accelerated by additional thyroid or anterior pituitary hormone and retarded by deprivation of these substances, and there is considerable experimental support for this belief. In addition there is a striking group of cases showing dental as well as other precocity in association with hyperplasia or neoplasms of the adrenal cortex.

The cases of Ogle (1865 *a, b*), Linser (1903), Gordon and Browder (1927), and Richardson and Doll (1939) and others show that the dental precocity may correspond to many years but is usually less than the apparent bone-age. The teeth are, of course, of normal size and the affection bilateral. It must be added that there are also cases of juvenile adreno-genital syndrome in which the state of formation and eruption of the teeth is nevertheless normal, such as that cited by Thoma (1943), suggesting that we are concerned not only with the presence of circulating hormone-like substances but also with considerable variations in the reactivity of the dental system towards them. It is unfortunate, however, that in the majority of the many cases of the syndrome reported the condition of the teeth is not described. The same is true of pineal gland tumours and other varieties of precocious development on record. We are all aware, of course, that precocious dentition may occur also to some extent in children who are in all other respects apparently normal, and that there is a difference between the means for the two sexes.

It has been known for many years that congenital hyperplasia of one side of the face or of the whole body may be accompanied by precocious eruption of the deciduous teeth on the same side; and in other cases it has been noticed that some of the teeth on the same side may be enlarged. It has been said that the latter condition—unilateral hyperplasia of the teeth—is one of the rarest of dental abnormalities, and reference books only note two or three cases. But the rarity is probably much exaggerated. It is likely that at least five such patients are living in the British Isles to-day: I have seen 3 and Sir Frank Colyer and Mr. A. E. W. Miles have each reported one. Since reported cases have never been collected and compared I thought it worth while to do this, the more so in that there is a remarkable resemblance in detail between the various known examples. It is evident that the abnormality develops according to some very precise laws, and even if one cannot say what they are it is worth examining their effects.

To begin with we must note that two different congenital disorders must be distinguished. In one there is hyperplasia of the whole or most of one side of the body including some of the teeth. Of this variety there are very few dental records. In the other kind the hyperplasia is confined to one side of the face only, including the teeth, and of this sort there are excellent dental records in certain cases. I shall chiefly refer to this group. It must be added that there is on record also a large number of cases of hyperplasia of one side of the body

I will illustrate the condition by mentioning some cases which I have been able to observe (two of them under the surgical care of Sir Harold Gillies) and will then discuss the dental features of the whole group of facial cases.

CASE I.—The patient was a boy of 5½ years in whom enlargement of the right side of the face had been noticed soon after birth (fig. 5). No other members of the family were malformed; and his health was good. The structures enlarged were the upper and lower lips, cheek, nostril, tongue, and ear on the right side, the upper and lower right alveolar processes; and certain teeth. The right side of the palate was wider, and the same side of the tongue carried globular elevations and appeared deficient in papillæ. The teeth erupted were $\frac{e43c21}{654321} | \frac{abcde}{1bcde}$ (fig. 6). The eruption of $\frac{432}{6543} | 1$ was incomplete, but in spite of this those on the right side were in contact with their opponents in the other jaw. $\frac{65}{7} | \frac{1234567}{234567}$ were present unerupted, but $\frac{7}{1}$ was congenitally absent.

The state of dental development of the left side was normal for the age both as regards calcification and eruption: that on the right showed in both respects a precocity on the whole equivalent to five or six years more than the real age. As regards size, comparison by measurement of homologous teeth on the two sides was only possible in the case of $e | e$ since the permanent teeth on the left were not erupted. $e |$ was very much enlarged: 12×14 mm. compared with 7.5×9.5 mm. on the left (normal mean: 9×9.5 mm.). By means of good radiographs and measurement of the erupted teeth the following conclusions were formed. The incisors were not enlarged, but the upper and lower right canines were enlarged and of abnormal shape, having the nipple-like tip described by Pagenstecher. The root formation of the lower canine was about seven years precocious but its



FIG. 5.—Case I.

[Reproduced by permission of the Editor of the *British Dental Journal*.]



FIG. 6.—Case I. Models after extraction of enlarged $e |$.

eruption only five. The premolars were probably a little larger on the right and the lower first molar certainly was so and had abnormal roots, the posterior one being strangely recurved. A similar root formation in the lower first molar was later described by Miles in his case. On the other hand the second molar was smaller than on the left though more advanced in development.

It is noteworthy that although $e |$ was huge the succeeding tooth $5 |$ was only slightly enlarged if enlarged at all.

CASE II.—The patient was a boy of 16 in whom enlargement of the face had been noticed at birth. No malformation was known to have occurred in the family. His general health was excellent. The head at the level of the eyes and above was symmetrical. The left cheek and the left side of both lips were enlarged but without undue pigmentation or hæmangiomas; and there were two button-like nodules on the lower lip (fig. 7). There was no difference in the hairiness or texture of the skin on the two sides. The left ear was longer and broader and about twice as thick as the right; it was also set a little lower. The malar bone and zygomatic arch were much more prominent on the left, but the anterior surface of the upper part of the maxilla and the infra-orbital border were symmetrical on the two sides. The body of the mandible on the left felt thicker from above downwards. Within the mouth, the anterior part of the tongue was much broader and rather longer on the left and was covered with irregular nodular and papillary elevations. The inner surface of the cheek and lower lip had also numerous soft polypoid excrescences, some an inch in width. On section these proved to be composed of connective tissue with rather numerous and large lymph vessels.

The alveolar processes of both jaws were much wider on the left, especially the upper, but in both cases were rather shorter on that side. The morphological mid-line of both jaws was deviated to the patient's right. Several of the upper teeth on the left were enlarged, the canine particularly (figs. 8 and 9). The teeth present and erupted were $\frac{7654321}{7654321} | \frac{123456}{123456}$; $\frac{8}{7}$ had been extracted. $\frac{8}{8} | \frac{7}{78}$

the dental conditions, though the various documents are not absolutely in agreement. The following teeth appear to have been present and erupted: $\frac{6e4321}{6e\ 321} \mid \frac{de6}{1cde6}$ The tooth occupying the expected position of $\overline{1}$ is probably $\overline{1}$ which has drifted across owing to its premature eruption. There were also three empty sockets from which $\overline{1bc}$ seem to have fallen out.

While the state of development on the left side is normal for the age, that on the right is precocious by two to four years. To some extent, therefore, Barwell may have been contrasting the "baby teeth" on the left with permanent teeth on the right. However, measurement from the scaled drawings and from enlarged photographs calibrated from the drawings shows that some of the teeth on the right were abnormally large. $e \mid$ seems to have been about 12×13 mm. (normal mean 9×9.5); and $e \mid$ about 12×12 (normal mean 10.5×8.7). $6 \mid$ also appears to have been very large, about 13×13 ; and $4 \mid$ was probably enlarged. It is impossible to say whether the upper canine was enlarged or not, but its shape appears abnormal and reminiscent of that found in some other cases.

The other teeth on the right, $\frac{21}{6321} \mid$, seem to have been within normal limits, though the shape of $\overline{6} \mid$ was abnormal and its enlargement cannot be excluded. Doubt must remain on some points, such as the nature of the small tooth which occupies the position of the upper left second deciduous molar.

Clerc (1904) reported another case in a boy who had been watched from 3 to 10 years of age. He was the first to state precisely which teeth were enlarged and which were not, among those visible to him. In particular he showed that of the deciduous dentition only the second molars were enlarged in his case. He also observed precocious eruption of the first dentition on the large side, and was the first to publish photographs of casts of the teeth in this condition.

Port (1904) and Werner (1905) described a further case. They published for the first time comparative measurements of the crowns of teeth on both sides, though not of all teeth. They also published the first radiographs of the facial bones in this condition, and these though very dim have some comparative value. In their case the frontal bone was among those enlarged, and excessive bone growth was still continuing in the malar region at twenty years.

Pagenstecher (1906) described a woman of 35. His case is noteworthy for some aberrations in form which he found in the teeth. Unfortunately he gave no measurements and his illustrations are very poor; but from the latter it seems probable that the upper lateral incisor was among the teeth enlarged, a thing only once recorded since.

These last 3 cases are the ones usually mentioned in reference books.

No further reports appeared until 1923 when Paterson and Reynolds recorded a probable case. The remaining case-reports, some detailed and some scanty, are by Colyer and Sprawson (1931), Masten (1936), Peyrus (1936), Rushton (1937 and 1942), Miles (1944), and Rudolph and Norvold (1944). I have since seen one further case but unfortunately not before most of the teeth had been extracted. Another probable case was published by Arnold (1936).

(Cases in which tooth enlargement was said to accompany hyperplasia of the whole of one side of the body were reported by Milne (1894), Arnheim (1898), Gesell (1921) and Wiseberg (1931).)

Altogether there are records of 19 cases in which there is probability or certainty that some teeth on the hyperplastic side were larger than those on the other. In 15 of these the facial region only was enlarged (11 male, 4 female; 7 right and 8 left). In 4 most of one side of the body was enlarged (1 male, 3 female; 3 right and 1 left). On the general question of asymmetry and tooth size we may note that Ballard (1944) found that of 500 normal persons 408 showed slight difference (0.5 mm. or more) between the diameters of some homologous right and left teeth.

As a general description of the condition one can say that the facial asymmetry is always noticed soon after birth. As the infant grows the disparity becomes more marked and it is presently found that some or all of the following parts on one side are enlarged: lips, cheek, anterior part of the tongue, ear, uvula, tonsil, nostril, upper and lower jaws especially as to the alveolar processes, teeth, malar bone, and sometimes the mastoid process and frontal bone. There are occasionally pigmentary and vascular abnormalities of the skin, or neurological disturbances.

The teeth may develop and erupt earlier on the enlarged side and some of them may also be enlarged: this applies to both dentitions. The asymmetry of the face may continue to increase as late as the age of 20 years: it varies from a relatively slight condition to the enormous disproportion seen in Barwell's case.

I will illustrate the condition by mentioning some cases which I have been able to observe (two of them under the surgical care of Sir Harold Gillies) and will then discuss the dental features of the whole group of facial cases.

CASE I.—The patient was a boy of 5½ years in whom enlargement of the right side of the face had been noticed soon after birth (fig. 5). No other members of the family were malformed; and his health was good. The structures enlarged were the upper and lower lips, cheek, nostril, tongue, and ear on the right side, the upper and lower right alveolar processes; and certain teeth. The right side of the palate was wider, and the same side of the tongue carried globular elevations and appeared deficient in papillæ. The teeth erupted were $\frac{e43c21}{654321} \mid \frac{abcde}{1bcde}$ (fig. 6). The eruption of $\frac{432}{6543} \mid 1$ was incomplete, but in spite of this those on the right side were in contact with their opponents in the other jaw. $\frac{65}{7} \mid \frac{1234567}{234567}$ were present unerupted, but $\frac{7}{7}$ was congenitally absent.

The state of dental development of the left side was normal for the age both as regards calcification and eruption: that on the right showed in both respects a precocity on the whole equivalent to five or six years more than the real age. As regards size, comparison by measurement of homologous teeth on the two sides was only possible in the case of $e \mid e$ since the permanent teeth on the left were not erupted. $e \mid$ was very much enlarged: 12×14 mm. compared with 7.5×9.5 mm. on the left (normal mean: 9×9.5 mm.). By means of good radiographs and measurement of the erupted teeth the following conclusions were formed. The incisors were not enlarged, but the upper and lower right canines were enlarged and of abnormal shape, having the nipple-like tip described by Pagenstecher. The root formation of the lower canine was about seven years precocious but its



FIG. 5.—Case I.

[Reproduced by permission of the Editor of the *British Dental Journal*.]



FIG. 6.—Case I. Models after extraction of enlarged $e \mid$.

eruption only five. The premolars were probably a little larger on the right and the lower first molar certainly was so and had abnormal roots, the posterior one being strangely recurved. A similar root formation in the lower first molar was later described by Miles in his case. On the other hand the second molar was smaller than on the left though more advanced in development.

It is noteworthy that although $e \mid$ was huge the succeeding tooth $5 \mid$ was only slightly enlarged if enlarged at all.

CASE II.—The patient was a boy of 16 in whom enlargement of the face had been noticed at birth. No malformation was known to have occurred in the family. His general health was excellent. The head at the level of the eyes and above was symmetrical. The left cheek and the left side of both lips were enlarged but without undue pigmentation or hæmangiomas; and there were two button-like nodules on the lower lip (fig. 7). There was no difference in the hairiness or texture of the skin on the two sides. The left ear was longer and broader and about twice as thick as the right; it was also set a little lower. The malar bone and zygomatic arch were much more prominent on the left, but the anterior surface of the upper part of the maxilla and the infra-orbital border were symmetrical on the two sides. The body of the mandible on the left felt thicker from above downwards. Within the mouth, the anterior part of the tongue was much broader and rather longer on the left and was covered with irregular nodular and papillary elevations. The inner surface of the cheek and lower lip had also numerous soft polypoid excrescences, some an inch in width. On section these proved to be composed of connective tissue with rather numerous and large lymph vessels.

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There was no record of the order of eruption of the teeth, but it is evident that the eruption of the two left second molars was retarded about four years already. With regard to size, in the upper jaw the incisors on the two sides are equal but the left canine is very large and of globular shape; it has no root. The left premolars are enlarged and have no roots, and the first molar is enlarged and has only one defective root. In the lower jaw the incisors on each side are equal, the left canine slightly larger. The second molar is smaller on the left.

The patient was re-examined in 1946 at the age of 21. The asymmetry of the soft tissues had in the meantime been greatly reduced by plastic surgery.

Radiographs of the facial bones showed no abnormality at the level of the orbits and above.



FIG. 7.—Case II.



FIG. 8.—Case II. Model of right upper teeth.



FIG. 9.—Case II. Model of enlarged left upper teeth.

The upper parts of the maxillæ do not differ much from each other; the left is probably a little wider and the right somewhat denser. The left malar bone carries an abnormal downward and outward prominence, and the left zygomatic arch is thicker. The left alveolar process of the maxilla has now increased in length and is of equal length with that of the right. The quality of the bone of the new-formed maxillary tuberosity is abnormal showing no cortex in intra-oral films. There is also an increased boss of bone posterior and medial to the first molar tooth. The latter, which previously only had one root, now seems to have lost this also. The mandible is rather more massive on the left side. Its canal is much enlarged and the mental foramen is twice the normal diameter (fig. 10). The second molar is still unerupted, and the third is not only unerupted but is covered



FIG. 10.—Case II. Radiograph of left mandible at 21 years.

by a proliferation of bone carrying an upward spur. The lower third molar on the right is now erupted. The hyoid bone appears equal on the two sides.

Comparing these with the previous findings one may say that an osteolytic process has destroyed the roots of the upper teeth from the canine backwards to the first molar on the left; that eruption on that side has ceased; and that abnormal bone apposition is proceeding on the posterior ends of the alveolar processes of both jaws. These are the parts in which one would expect still to find some bone growth at this age, but of quite a different kind and connected with the eruption of the third molars.

CASE III.—In a third case, a young woman under the care of Mr. Patrick Clarkson, most of the teeth had already been extracted but the other deformities, including in this instance the frontal bone, were well shown.

The following are some of the principal dental findings in the whole group of facial cases.

(a) *Size.*—Of the deciduous dentition only the second molars are known to have been enlarged and then only in 3 cases (Barwell; Clerc; Rushton, 1937). In Clerc's case the other deciduous teeth were normal but in most cases none remained at the time of examination owing to their very early loss on the large side.

The greatest enlargement found amongst the permanent teeth occurs in the canines and does not exceed an increase in diameter of 50%; next in the first molars and first premolars; then in the second premolars. The upper central incisors are never enlarged which may be connected with their development in tissue derived from the fronto-nasal process. The upper lateral incisors and the lower incisors are rarely enlarged and then slightly. A second molar has only once been found enlarged (Colyer) and these teeth are sometimes smaller than those on the normal side. Little is known of the condition of the third molars.

(b) *Rate of development.*—Eruption of the deciduous teeth may be and perhaps usually is precocious to the extent of several months on the large side. And precocious eruption of the permanent teeth on that side is usually a striking feature: there may be a precocity of five years at the real age of 5 or 6. After that age it diminishes; and in some cases the eruption of those teeth which should normally erupt late, the second and third molars, is retarded compared with normal expectation or fails completely. It is estimated that in these cases a retardation of eruption has begun before the age of 10 years. The state of formation of the teeth is comparable with the state of eruption at any time except in the case of the second and third molars where any retardation of eruption is not accompanied by retarded formation. In contrast with the distribution of size-abnormality those teeth which are formed in tissue derived from the fronto-nasal process and those formed in tissue derived from the first visceral arch are equally affected as regards accelerated formation and eruption. It is also clear that this acceleration affects indifferently those teeth on the large side which are hyperplastic and those which are not. The second molars may show accelerated formation even though their size be diminished; or a normal state of formation though their eruption be retarded.

(c) *Alveolar bone.*—The distribution of areas of increased and diminished growth of alveolar bone is usually the same as that of areas in which accelerated and retarded eruption occur, and does not correspond closely with the distribution of tooth enlargement. The alveolar bone growth is not only precocious but also excessive and disorderly. Abnormal absorption of tooth roots has been reported in 2 cases (Rushton, 1942; Miles, 1944).

(d) *Tooth form.*—The enlarged teeth often have an alteration in form as if they had been inflated. This may be due to a greater overgrowth of the mesodermal than of the ectodermal elements, a thing several times observed in other organs at autopsy in cases of partial gigantism (Hornstein, 1893; Arnheim, 1898; Cagiati, 1907).

The various hypotheses which have been put forward to explain the syndrome of congenital unilateral hyperplasia as a whole have been summarized by many authors and recently by Schwartzman, Grossman, and Dragutsky (1942). Of these the suggestions of chromosome or gene abnormalities probably accord best with the dental evidence.

I am not competent to discuss the nature of such a genetic defect: reference to such a paper as that of Grüneberg (1935) shows that the number of possible interpretations of asymmetrical development is large. Suggestions of somatic mutation and of non-disjunction have been made, but there is one record (Rudolph and Norvold, 1944) which claims that the facial enlargement, though not necessarily that of the teeth, was present in three generations, and if this was so those suggestions are not likely to be correct. An alternative is to suppose a hereditary factor with a very low manifestation rate.

The distribution of the whole abnormality corresponds to a considerable extent with that of structures derived from the first visceral arch but the correspondence is not precise: areas outside that zone are often affected and some areas and teeth within it are not. If the malformation be considered an abnormal gene effect it is one of the diffusely localized variety. The localization in respect of increased organ-size and of precocity is not exactly the same in extent: and these two abnormal influences are effective at different periods—

were present unerupted and $\bar{8}$ was congenitally absent. One cusp only of $\bar{7}$ had erupted in an abnormal position on the medial side of the alveolus.

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[February 2, 1948]

Smallpox 1947. [Abridged]

By W. H. BRADLEY, D.M., M.R.C.P.

DURING 1947 the diagnosis of smallpox was confirmed in 79 persons infected in England and Wales. 15 of these died. Although the numbers are small the experience deserves comment for three reasons. First, the number of cases was the highest since 1934 when there were 179, mainly of variola minor, with 6 deaths only. Secondly, we must recognize the great importance of the fact that in 1935 endemic variola, both major and minor, had completely disappeared from these Islands. During 1947 in one area of Staffordshire the infection persisted through nine generations and at one time there appeared to be a real threat that smallpox might again establish endemicity. Thirdly, the experience was sufficiently small to permit some close-up observations from which there are some lessons to be learnt.

In each of the years 1939, 1940, 1942, 1944 and 1945 there was a single importation of smallpox. In 1946, in consequence of the return of our Forces from the East, there were 15 importations (discussed by Boul and Corfield 1946, Peirce 1947, Conybeare 1946, Stallybrass 1947). In 1947 there were two importations; the source of the first was not proved, the second originated in India. The geographical spread is discussed elsewhere (Murray and Bradley, 1948).

FIRST IMPORTATION

Two old men, aged 85 and 75, resident in a common lodging house at Grimsby, became ill on February 8 and 13 and were subsequently diagnosed in the Public Assistance Hospital as smallpox. When lists of contacts were made several of the mariners and tramps who frequented the lodging house had disappeared. There is little doubt that amongst them was the source case. It may be significant that at the time an unprecedented blizzard virtually isolated Grimsby by road and rail for several days and that vessels from French ports were lying at Grimsby. A case of smallpox was reported from Paris with onset on February 10 and 32 cases followed there as well as cases in other parts of France. Also among those who disappeared was the unknown man who transported the disease to Stepney where a resident member of the staff of a seamen's hostel (273 beds) sickened on March 3. He was removed from the hostel before the rash appeared but was in a ward of an East London general hospital till March 9 when a pustular rash was diagnosed smallpox. Contact listing, surveillance and vaccination were speedily undertaken and only one secondary case occurred in a contact under observation in the hospital.

At Grimsby there were 13 cases in the second generation, 2 being in members of the Public Health Department staff, others in contacts in the Public Assistance Hospital and in the inmates of the lodging house. Some of these inmates absconded from surveillance. Two moved to a dosshouse in Scunthorpe, 28 miles from Grimsby, where on March 2 a permanent resident developed a rash. He was removed to the infectious diseases hospital on March 25 as a case of chickenpox. It may be assumed that suspicion of smallpox arose because material was sent to the laboratory, but no precautionary measures other than isolation were taken nor was a second opinion consulted until after the laboratory reported variola virus present on April 1. Subsequent cases included 4 inmates of the common lodging house, a nurse in the infectious diseases hospital and the Acting Medical Officer of Health. Once again tramps from the lodging house absconded and were probably the means of conveying the virus to Doncaster and Barnsley. It was found that tramps moved between these towns and London by jumping lorries.

increased size from before 5 or 6 months of foetal life until perhaps 1½ to 2 years, and precocity from birth until 9 or 10 years with a maximum at 5 or 6.

The precocity which occurs is of the same order as has been found bilaterally in some endocrine disturbances but in facial hemihyperplasia there is no evidence of any excess of such hormones and the contralateral teeth are normal. It appears reasonable to think that such an abnormal effect may operate through an abnormal reactivity in the affected area to normal influences promoting growth at any time, and that the normal variation in these may determine the very different effects produced at different age-periods. States in which there is failure of localized areas to react in the expected manner to various hormones, whether bilaterally or not, are recognized, also the different reactivity of various parts at the same or different times. Dana's case (1893) of acromegalic gigantism in which the whole body except one side of the face was affected could be regarded as a kind of opposite to the cases here discussed.

It appears that in these cases of facial and dental hemihyperplasia we see the result of removal of one or more of the factors which normally control in a certain area the rates of cell-proliferation and of morpho-differentiation and the relationship between the two determining in the normal environment the ancestral rate of development and size of the dental organs. Perhaps the most surprising thing is that among so many known genetic abnormalities in this one almost alone in man can enlargement of the crowns of a series of teeth occur, and then only during a period of two or three years. While variations in tooth number and partial dichotomy or partial fusion are common, also such modifications of growth gradients as will produce either increased complexity or extreme simplification of form, the upper limit of size of teeth of approximately normal pattern seems most insusceptible to either environmental or genetic disturbance.

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increased size from before 5 or 6 months of foetal life until perhaps 1½ to 2 years, and precocity from birth until 9 or 10 years with a maximum at 5 or 6.

The precocity which occurs is of the same order as has been found bilaterally in some endocrine disturbances but in facial hemihyperplasia there is no evidence of any excess of such hormones and the contralateral teeth are normal. It appears reasonable to think that such an abnormal effect may operate through an abnormal reactivity in the affected area to normal influences promoting growth at any time, and that the normal variation in these may determine the very different effects produced at different age-periods. States in which there is failure of localized areas to react in the expected manner to various hormones, whether bilaterally or not, are recognized, also the different reactivity of various parts at the same or different times. Dana's case (1893) of acromegalic gigantism in which the whole body except one side of the face was affected could be regarded as a kind of opposite to the cases here discussed.

It appears that in these cases of facial and dental hemihyperplasia we see the result of removal of one or more of the factors which normally control in a certain area the rates of cell-proliferation and of morpho-differentiation and the relationship between the two determining in the normal environment the ancestral rate of development and size of the dental organs. Perhaps the most surprising thing is that among so many known genetic abnormalities in this one almost alone in man can enlargement of the crowns of a series of teeth occur, and then only during a period of two or three years. While variations in tooth number and partial dichotomy or partial fusion are common, also such modifications of growth gradients as will produce either increased complexity or extreme simplification of form, the upper limit of size of teeth of approximately normal pattern seems most insusceptible to either environmental or genetic disturbance.

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VACCINATION

Vaccination did not fail us although it was used sparingly. In spite of some uncertainty at times concerning the prospect of control of the Bilston outbreak by surveillance and vaccination of contacts alone, the Ministry of Health's Medical Officers did not advocate mass vaccination. A high proportion of the population chose to be vaccinated and this may to some extent have affected the course of the outbreak. Yet I believe that the Ministry's advice was sound and am very doubtful about the statement made by the Commissioner of Health for New York City that "whenever a case of smallpox occurs in a community the only safe procedure is for every person in that community to be vaccinated without delay" (Weinstein, 1947). All the 12 patients in the 1947 outbreak in New York were in the direct line of contact and the outbreak terminated with the second generation of cases. 9 of the patients were unvaccinated and 3 had been vaccinated more than forty years previously. It is difficult to see how the mass vaccination of some 6 million New Yorkers affected the outcome. Vaccination on this scale was a remarkable achievement but any benefits which accrued must be set against a serious disadvantage. 50 cases of post-vaccinal encephalitis were reported and in 46 the diagnosis was considered probable; 8 of these died and 3 other deaths were reported from complications of vaccination. Weinstein comments "tragic as these incidents were, it must be borne in mind that had vaccination not been carried out, there very likely would have been thousands of cases (of smallpox) and hundreds of deaths". Our experience in this country suggests that it was not very likely, and past history confirms that the evolution of an epidemic of smallpox is relatively slow (Bradley, 1947).

COMMENTS

There was a difference between the outbreaks resulting from the two 1947 importations. In the Grimsby series the difficulty of handling the freedom-loving tramps led to dispersal over a wide area. Nevertheless, early detection and removal of cases together with vaccination and close surveillance of contacts brought control within two generations at each of the foci which resulted and it was possible to conjecture the route of spread except in the one late case at Barnsley.

In Staffordshire, on the other hand, the great difficulty in diagnosing the highly modified disease in the early cases and hesitation in accepting a laboratory diagnosis postponed action until thirty-four days after the onset in the original case. Although the disease remained confined to adjacent towns, nine generations of cases occurred before it was controlled and the route of spread to many cases could not be discovered.

The first lesson to be learnt is that if Wanklyn's question "Can this be smallpox?" cannot be answered with a firm negative, suspicion remains and routine smallpox precautions must start immediately. The second lesson is the great value of the Public Health Laboratory Service Smallpox Reference Laboratory at Colindale. A positive report from the laboratory must on no account be ignored. (A negative report must be treated with reserve if clinical suspicion remains.) Other lessons are: vaccinate everyone who enters a smallpox hospital, see that lists of contacts are comprehensive and make surveillance the main line of defence. Do not expect vaccination after contact to overtake the established infection or eliminate all risk of infectivity. Lastly, look to the vaccinal state of Public Health staff and ensure that contacts among them submit to surveillance no less rigorous than that applied to the general public.

So long as homing Britishers move around the world these Islands are at risk from imported smallpox, and we must aim at a high level of immunity obtained by routine infant vaccination with re-vaccination at suitable intervals. The appearance of the virus here should not be the signal for panic mass vaccination. Rather should all our resources, which are by no means limitless, be thrown into that reconnaissance,

Doncaster's singleton case was an assistant master at a preparatory school. The onset of his illness was sufficiently severe to send him to bed but clinical diagnosis of his highly modified rash was difficult and became confident only after laboratory examination.

At Barnsley the original source of infection was probably present in a common lodging house occupied by 93 men, women and children from April 30 till May 7. This focus of infection was detected only when it was found that a case with an early rash diagnosed in Bermondsey on May 16 had stayed at a common lodging house in Barnsley on the conjectured date of infection. Inquiries revealed 3 persons with early rashes, 2 in the lodging house and 1 in the Municipal Hospital. The inmates of the lodging house were immediately vaccinated and after 2 more cases in the first wave, making a total of 5, there were only 2 in the second wave. Despite extraordinary efforts to keep the residents together a few tramps absconded. They were probably the source of infection of an isolated case at Wakefield and possibly carried the infection to Sheffield. In the Municipal Hospital at Barnsley there were 5 secondary cases in ward contacts. One of these was in a child admitted for one night only and discharged on May 16 when the smallpox scare started. The parents refused vaccination. This case illustrates the importance of making comprehensive lists of contacts. The last case in Barnsley occurred a month after the last case in the town outside any known line of contact and within half a mile of the hospital. This type of unexplained case near smallpox hospitals seems to occur more frequently than could be due to chance (Millard, 1944).

The singleton case at Wakefield was in a night watchman who frequently entertained vagrants round the fire in his hut. Vaccination of contacts in the lodging house where he lived was performed early and their surveillance was relatively easy.

The primary case in Sheffield was in a child of 11 years who was confined to bed on May 1, developed a rash on May 4 and was diagnosed and removed only on May 9. Vaccination at this time could offer little protection, and the contacts, all members of the family, were persuaded to enter a quarantine house. The father and an aunt, both unvaccinated prior to contact, later developed the disease. The cost of the quarantine house was amply justified.

SECOND IMPORTATION

An Army sergeant arrived from India at Heath Row by air on February 23 and proceeded to his home at Bilston in Staffordshire on the next day. On March 1 he was unwell but remained ambulant until a rash was reported on March 6. Expert opinion diagnosed chickenpox both in this patient and in his mother and a visitor to the house who developed rashes on March 21 and 25. On April 1 material was sent to the laboratory where variola virus was found to be present, but the experts remained incredulous. Contacts were vaccinated on April 3, and 2 who were then ill developed rashes on April 5 and 7. Only on April 8 were routine smallpox precautions put into operation. The development of this outbreak to involve 24 cases and its spread to the contiguous district of Coseley (4 cases) have been described by Simpson Smith (1948).

A few interesting points can be added. Despite careful investigation the line of spread into 8 of the 13 families could not be discovered. In two instances the link in the chain of infection was not a diagnosable case of smallpox but was nevertheless a human being. Healthy carriers may occur although there is ample epidemiological evidence that they and cases of variola sine eruptione are much less infectious than patients with the exanthem. A singleton case from Dudley reported by Simpson Smith (1948) as a case of relapsing smallpox was more probably a hospital infection. The patient had been vaccinated in infancy forty-five years previously and was not revaccinated on admission to the smallpox hospital. The only case exported from the Bilston area was in a medical student at Birmingham who was allowed to see the cases without being adequately protected by recent vaccination.

They were able to show that the causal factors include sustained malnutrition or ill-health and poor posture, and that the disease is closely related to the geographical distribution and incidence of dental fluorosis. There is some evidence that those who are affected derive benefit from a better diet and improved social conditions.

Dr. W. T. Russell briefly reviewed the importance of the statistics of occupational mortality and indicated the greater precision now made by the Registrar-General in their evaluation. Having stressed the care necessary in their interpretation, especially on account of the possible influence of selective physical recruitment to particular occupations, he then emphasized the importance of industrial accidents since they represent direct occupational risks. He gave figures from the Chief Inspector of Factories' Annual Report, 1945, which indicated that there were 223,000 reported accidents in that year, and quoted the Chief Inspector's statement on the action deemed desirable for their prevention.

He described an investigation now being made at the Institute on the incidence of accidents in the three large factories in the Oxford Area. All accidents, minor and major whether involving lost time or not, are included in this study. Slides illustrating the statistics of the injuries, their type, causal agents and the correlation between incidence and age of worker were shown.

Dr. Russell concluded by indicating the broad character of this study which is a co-operative effort by the factory doctors, safety engineers and the Institute, in which they aim also to correlate the sickness records of the workers with their accident statistics, in the hope that further light may be shed on accident proneness.

Dr. Alice Stewart and Dr. J. P. W. Hughes: Mortality statistics over the last fifty years were given which showed that there is an excessive mortality from pulmonary tuberculosis in the boot and shoe industry, corresponding with the high morbidity rate found in a recent mass radiography survey in Northamptonshire (Smith, C. M., 1946, Northamptonshire County Council, Mass Miniature Radiography, 1945-1946, S. L. Hunt, Rushden, Northants).

The present survey was planned in order: (1) to exclude effects likely to be caused by home, racial, familial or immunological considerations; (2) to discover whether there were specific factory conditions which might account for the high incidence of the disease.

The findings in respect of the first part of the investigation suggest that boot and shoe factory operatives differ little if at all from other factory workers in the county. The second part of the investigation revealed both evidence of selective recruitment into the industry and the presence of unfavourable working conditions. For instance, examination of nearly ten thousand health records of men called up into the Services revealed a lower proportion of physically fit men in the boot and shoe industry as compared with other factory workers in Northamptonshire and Leicestershire. Secondly, working records of men known to have had tuberculosis showed that these men are more often employed in the boot and shoe industry than in other trades in Northamptonshire.

Further analysis of the mass radiography records possessed by Dr. Smith showed that workers in the large boot and shoe factories contracted the disease more frequently than workers in small factories, and that there was a close relationship between size of factory and the incidence of pulmonary tuberculosis. There was no evidence that this was due either to differences in sex and age of the factory populations or to the factories being situated in towns or villages. It was concluded, therefore, that size of factory (and hence size of workshop) was the main factor determining the incidence of tuberculosis.

Some of the factories had already been graded into good, fair and poor by the factory inspectorate. When the "factory grade" was compared with the tuberculosis morbidity rates it was found that although the poor factories produced

clinical and epidemiological, which reveals the distribution of the virus and enables us to apply deliberately, step by step, calculated counter-measures. This and the public demand for vaccination will keep us busy enough.

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[April 23, 1948]

MEETING HELD IN THE INSTITUTE OF SOCIAL MEDICINE, OXFORD

SUMMARY

Professor J. A. Ryle, in an introductory talk, described the origins and purposes of the Institute, which was opened in April 1943. He and his staff were predominantly occupied with socio-medical research programmes, but they had also assumed responsibility for undergraduate teaching during the first clinical year. The course included (1) lectures on the historical and theoretical aspects of the subject by himself and his immediate colleagues; (2) lectures on public health practice, industrial medicine, epidemiology and social case-work by members of the local health departments, a factory medical officer, the public health bacteriologist and the senior almoner of the Radcliffe Infirmary; (3) eight classes in medical statistics; (4) socio-medical case-conferences; and (5) field visits. Approximately fifty hours were devoted to the course. Wherever possible the close inter-relationships of clinical and social medicine were stressed.

The main sections of the Institute were concerned with: (1) Occupational Disease and Hygiene (the Assistant Director, Dr. Alice Stewart); (2) Child Health (Dr. Cicely Williams); (3) Student Health (Dr. R. W. Parnell); (4) Vital Statistics (Dr. W. T. Russell); (5) Radiology (Dr. F. H. Kemp). Reference was also made to the associated Bureau of Health and Sickness Records (Mr. H. Cotton).

The investigations undertaken were, in the main, epidemiological and ætiological and were based upon a variety of surveys, involving collaborations between physicians, statisticians, a medical social worker and a radiologist, on the one hand, and others in the fields of public health, industrial medicine, the school medical service, the maternity and child welfare services, &c., on the other.

Current researches included (1) a study of health and sickness experience and growth in the pre-school child, based upon a sample of upwards of 500 babies drawn from all social groups; (2) a study of student health; (3) an investigation into the high rate of tuberculosis in the boot and shoe industry; (4) sickness and accidents in factories; (5) hospitalized accidents; (6) the morbidity and mortality of appendicitis; (7) the health of the housewife.

After brief discussion the meeting was later resumed and short communications were given by Dr. F. H. Kemp and Dr. D. Wilson (*Social and nutritional factors in juvenile osteochondritis of the spine*); by Dr. W. T. Russell (*Occupational morbidity and accidents*); and by Dr. Alice Stewart and Dr. J. P. W. Hughes (*Tuberculosis in the boot and shoe trade*).

Dr. F. H. Kemp and Dr. D. Wilson reported a series of investigations which they had conducted into the ætiology of osteochondritis of the spine (Scheuermann's disease).

it becomes common. A similar series was also collected without difficulty in a general military hospital in England during the next winter (Copeman, 1942) in the absence of any outbreak of meningitis.

Peripheral mononeuritis.—Another outbreak of which the symptomatology was at first considered to be rheumatic was described by Spillane (1943) who pointed out that although polyneuritis with the exception of the diphtheritic form was rare in the M.E.F., a number of cases of paralysis, mostly affecting single muscle groups, were being seen in the military hospitals. The groups affected were mostly those of the shoulder girdle. Such cases had not been observed before the war, so far as he was able to ascertain. The cases seen fell into two groups; in the first the affection of the shoulder girdle developed while the patient was in hospital convalescing from some other illness. Sometimes they had even been transferred to a convalescent depot, and always they were afebrile. No common causative factor could be detected and evidence of faucial or cutaneous diphtheria was lacking. In the second group, the illness began whilst the victim was on duty with a sharp pain in the shoulder which sometimes radiated down the arm, and which lasted up to fourteen days, after which weakness and later wasting became prominent. In most cases this wasting became considerable and Spillane records that he never saw any certain regeneration of muscle in such cases, although improvement occurs in milder cases.

The uniformity of the clinical findings in this and similar series seems to suggest, although it does not prove, a common causation. In respect of these patients, two considerations spring to mind: first the number of injections to which their upper arms had probably been subjected, and the ever-present possibility of trauma in soldiers on active service. In connexion with this latter condition, Spillane states that he never saw a typical case in an officer, although such have been recorded. The differential diagnosis was chiefly from localized poliomyelitis, but pathological investigation established its difference. As the result of much further investigation it was concluded that neither severe injection nor trauma was causative. No certain aetiology can therefore as yet be invoked for these cases which later were seen in many theatres in the war.

Jaundice.—Infective hepatitis, with a small mortality, constituted, after malaria, one of the principal man-power problems which confronted us in the Middle East and the C.M.F. The epidemiology of this condition has never been established with certainty, and each outbreak encountered, therefore, presented a fresh challenge to the amateur epidemiologist. The accepted method of spread of infective hepatitis has always been by droplet spray amongst close contacts, or even personal contact; this could but rarely have been the case, however, in the outbreaks noted amongst units and individuals scattered about the deserts of the M.E.; whilst the extreme rarity with which, if ever, it appeared to be transmitted to nursing sisters seemed also to throw some doubt on this method of transmission. Wits (1944) in reviewing this problem as it appeared amongst the troops around the Mediterranean, where the disease is endemic, did not discard the belief prevalent amongst the troops that a potent cause was imperfectly washed communal crockery. This hypothesis was thought by many M.O.s on the spot to explain the increased incidence of the disease noticed amongst officers as compared with men. Findlay and Willcox (1945) later produced typical cases in volunteers following the oral ingestion of faeces or urine from spontaneous cases, which seems to favour the view, to which I personally found myself attracted by the evidence, that an insect vector must be the transmitting mechanism.

It was during the late war also that post-inoculation jaundice was established as an entity *sui generis*. Findlay, summarizing the evidence in 1940, decided that the agent, although probably differing from the filtrable virus believed to be the cause of infective hepatitis, is of the same nature. Later he proved that this agent was present in the nasal secretion of sufferers amongst the N. African Force, and was

more cases than the good factories, this effect was not sufficient to overcome the effect of size; for instance, in a "poor" small factory the incidence of this disease was less than in a "good" large one, whilst in the "poor" large factories the incidence of the disease was higher than in any other group.

After further discussion demonstrations were given (1) of recording methods and the design of record cards for survey work, and (2) of the Powers-Samas Machine Room.

[May 3, 1948]

Clinical Epidemiology

PRESIDENT'S ADDRESS

By W. S. C. COPEMAN, O.B.E., M.D., F.R.C.P.

EPIDEMIOLOGY is the study of disease prevalent amongst communities at special times, and was initiated by the Father of Medicine himself when he observed that certain climatic variations were associated with certain prevalent diseases (Hippocrates, Epidemics i and iii). Epidemiology has in all ages perforce been a major interest of the physician, but it became developed as a special branch of Medicine with the evolution of the scientific method which was introduced by Harvey and John Hunter, and later, with the application of statistical methods to medical practice, by pioneers such as Snow and William Budd. Since the middle of the last century it has tended to be regarded exclusively as a branch of Public Health and the professional epidemiologist is now rightly regarded as an important unit of the team responsible for the corporate health of the community.

In isolated districts, and more particularly in time of war, small communities often find themselves circumscribed in medical conditions in which epidemiological knowledge and technique are desirable. It not infrequently happens, however, that the situation has to be handled by someone trained only in clinical medicine. We need only turn to the communications of Pickles prior to the late war (many of them to this Section) to realize that even in such circumstances our knowledge has not infrequently been advanced.

It is to such a combination of circumstances that I apply the term "Clinical Epidemiology", and it is mostly to some personal wartime experiences that I propose to refer.

Chronic meningococcal septicæmia.—During the winter of 1939–40, during the period of the "phoney war", some cases were noticed in one of the tented hospitals in France which presented an acute pyrexial onset followed rapidly by severe migratory joint and muscle pains often with effusion, and in most cases followed by a somewhat inconspicuous rash, which sometimes however simulated erythema nodosum. They mostly ran an irregular or remittent fever subsequent to the onset. In spite of all this, the patients rarely seemed to feel seriously ill. It was found that sulphonamides were a prompt and effective remedy, which cast doubt on the diagnosis of rheumatic fever or influenza, with which they had mostly been admitted. At this time a small epidemic of meningococcal meningitis had been reported in the Army. In view of the association of chronic meningococcal septicæmia with acute outbreaks of meningitis in America reported by Appelbaum (1937) and by Binns and Clancy (1939) in children, a series of blood cultures was undertaken in these cases. This resulted (not without difficulty) in positive cultures for this organism being obtained in some 17 of the cases within a period of nine weeks. These cases were carefully analysed (1940) by Stott and Copeman who stated their belief that chronic sporadic meningococcal septicæmia, although not widely recognized, is not rare, but that whenever meningococcal meningitis is prevalent in a community

it becomes common. A similar series was also collected without difficulty in a general military hospital in England during the next winter (Copeman, 1942) in the absence of any outbreak of meningitis.

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The uniformity of the clinical findings in this and similar series seems to suggest, although it does not prove, a common causation. In respect of these patients, two considerations spring to mind: first the number of injections to which their upper arms had probably been subjected, and the ever-present possibility of trauma in soldiers on active service. In connexion with this latter condition, Spillane states that he never saw a typical case in an officer, although such have been recorded. The differential diagnosis was chiefly from localized poliomyelitis, but pathological investigation established its difference. As the result of much further investigation it was concluded that neither severe injection nor trauma was causative. No certain ætiology can therefore as yet be invoked for these cases which later were seen in many theatres in the war.

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able to transmit the disease to three volunteers by the instillation of washings into their nares.

Another type of jaundice, which follows the injection of arseno-benzine preparations, was also much seen, particularly in the Italian campaign where the V.D. rate was high. It seemed from the careful reports of the local M.O.s that this type was probably transmitted by imperfectly sterilized syringes or needles being used for the injection of arsenicals into successive patients. This view has now been generally adopted. (Medical Research Council War Memo. No. 15, 1945.)

In all cases of jaundice occurring in endemic areas, it is obviously very important to exclude Weil's disease, and the story of its identification in the B.L.A. in France and Holland has been told by my colleague Dr. E. Bulmer (1945). The occurrence of the disease had not been unforeseen in view of the known presence of rats which had been found to harbour the spirochæte in the urine and the conditions which were prevalent in the earlier part of the campaign. The first case to be recognized occurred in Caen in July 1944, and the report which was at once circulated to all physicians in the Force rendered the arrival of each case of jaundice something of an adventure. In all, Bulmer estimates that about 100 cases must have occurred, although as some were without jaundice more may have been missed. It seemed that the source of infection was almost certainly the water which was used by the men for washing, since all drinking water was sterilized by the usual efficient Army methods. For washing, the men were forced to draw water from the wells and streams. It is, however, probable that they also cleaned their teeth in such water. Bathing in the streams was allowed, the alternative—if it could have been enforced—was that the men should remain dirty and unrefreshed during the rather dreary period prior to the advance, during which it was often exceedingly hot. On some sectors they perforce lived in damp rat-infested ditches and the risk, such as it was, was taken therefore advisedly. It is interesting to note in this connexion that the leptospira isolated in this outbreak were found by Brigadier J. S. K. Boyd to be moderately penicillin-sensitive, and subsequent treatment of some 36 cases with this substance yielded results which were thought to be worthy of further and more extended trial.

Epidemic myalgia.—Bornholm disease has generally been considered as the only recognized example of an infective myalgia. During the winter 1940–41, however, a number of cases of "fibrositis" were seen from a single isolated military unit. All these cases were of similar onset and type and affected the neck, shoulder-girdle, and arms of the sufferers. On further investigation it appeared that the condition showed some signs of being of an epidemic nature. About that time the American Harvard Red Cross Unit arrived under the charge of Dr. (now Professor) Paul Beeson whose assistance was sought in this matter. Subsequently to this he and his team investigated in all four similar outbreaks during 1941–42. He described the results of this work before this Section the same year, and included the cases which actually occurred within his own staff. I will quote some of his observations on the epidemiology of this interesting and unusual investigation. In October 1941 several cases of "stiff neck" occurred among members of the staff of this unit. All persons in the community were therefore canvassed in order to determine the prevalence of the condition. This revealed that a considerable number of persons (up to 24% of those who were resident) had suffered an attack of myalgia in the neck or shoulder regions within the preceding two months period. Similar cases of myalgia were reported in a near-by factory and also among a unit of A.T.S. billeted in the neighbourhood. Systematic inquiries revealed a recent high incidence of acute myalgia in these two groups. A fourth survey was then made amongst a detachment of soldiers, and the incidence of myalgia in that community was found to be considerably less than that in other groups. A full study was made of these four groups and it was concluded (Beeson and Scott, 1942) that the evidence obtained indicated that

the prevalence of the condition fluctuated in a manner similar to that of communicable disease, and certain types were defined. Most affected persons had a mild self-limited illness of fairly uniform course, but occasionally the disease passed into a chronic form and extended to other parts of the body, and eventually produced the clinical syndrome of generalized fibrositis. These chronic cases would not ordinarily be identified as having originated from an epidemic of benign myalgia of the neck. Transmission experiments seemed to promise some success but were not, by the time the unit disbanded, conclusive. It will be seen therefore that the evidence of this investigation supports the concept that acute "fibrositis" of the neck and shoulders may sometimes present as an infectious disease. This work should undoubtedly be followed up and repeated.

A further very small epidemic which occurred elsewhere and was independently reported by Houghton and Jones (1942) may be quoted, as the occurrence of epidemic forms of fibrositis is not well known. Seven members of the nursing staff of a hospital developed sore throat, this was followed in eight to eleven days in six of them by severe pains in the muscles and headache. These pains and some mild pyrexia persisted for up to five months, menstrual disturbances and spontaneous epistaxis were also reported although the E.S.R. remained normal throughout. The explanation put forward by the observers was that the condition was due to a myotropic strain of virus, although no extensive epidemiological investigations were made in this outbreak. Other rather similar outbreaks are on record, and two others are within my own recollection, although unpublished.

Cutaneous diphtheria.—Northern Palestine was, in 1941, an area where the skin lesions known as desert sore had become increasingly frequent and Cameron noted that this rise had coincided with a small outbreak of faucial diphtheria. Craig had reported in 1919 that a large proportion of cases of desert sore investigated by him in the Sinai Peninsula were found to yield the Klebs-Löffler bacillus, and Cameron therefore undertook an investigation with Muir (1942) into the cases of desert sore in his area. He found that the unit showing the highest incidence of this affection was a Yeomanry Regiment. Soon after arrival from England during June-August 1940, 12 cases of faucial diphtheria had broken out in the unit. After this a carrier had been found and after his isolation no further trouble had been reported. Both before and after this outbreak, desert sores were reported to be numerous in the unit. Subsequent to the diphtheria outbreak, however, swabs and scrapings were taken from the bases of the ulcers after removal of the overlying scabs, and the presence of the diphtheritic bacillus was proved in 66 cases. Later this state of affairs was shown to exist in all parts of Palestine. When this report was circulated, my unit was in the desert south of Baghdad, and as 40 cases of desert sore were at that time in hospital, they were immediately investigated on the same lines, with the discovery of the Klebs-Löffler bacillus in 28 of these cases, although no clinical differentiation from non-diphtheritic-infected sores seemed to be possible. In 2 of the cases mild palatal paralysis subsequently developed after the sores had healed. This had also occurred in a number of Cameron's cases, and a knowledge of the preceding epidemiological investigation thus explained what would otherwise have become an obscure neurological problem. The routine use of diphtheritic antitoxin in all intractable cases after 1942 served to prevent a recurrence of this problem.

Typhus broke out in Naples at the end of 1943. It was here that louse-borne typhus, from time immemorial the scourge of every combatant army, met its Waterloo in the shape of the then newly invented D.D.T. The 1946 edition of the Army Manual on medical diseases of the tropics states as the result of this experience that "There is now no reason why a properly equipped modern army need fear typhus".

It is generally accepted since the work of Mackenzie (1941) that the appearance of the exanthematic variety of typhus in a community is due to the previous existence

able to transmit the disease to three volunteers by the instillation of washings into their nares.

Another type of jaundice, which follows the injection of arseno-benzine preparations, was also much seen, particularly in the Italian campaign where the V.D. rate was high. It seemed from the careful reports of the local M.O.s that this type was probably transmitted by imperfectly sterilized syringes or needles being used for the injection of arsenicals into successive patients. This view has now been generally adopted. (Medical Research Council War Memo. No. 15, 1945.)

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(h) A well-equipped organization is essential. Adequate staff, equipment, and transport must be available.

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Dr. Oswald Savage referred to the excellent work done by the Americans in Naples in combating typhus. They split up their team of typhus workers into three sections. The first was a diagnostic section which went out and ascertained that a given case was typhus. The second section surrounded the plague spot and sprayed everybody in the tenements and dwellings. The third section rounded up the inhabitants of Naples and got them into shelters and other places and sprayed them before they were allowed in the streets again. In the British hospitals at Naples a team went round once a week to spray all civilians. Only one case of typhus, he believed, was reported in the troops, and that was in a soldier who broke out of gaol and was missing for forty-eight hours.

Dr. Allan McFarlan referred to the transmission of the virus in infective hepatitis. Personally he felt inclined to think that in infective hepatitis the virus might be transmitted from the faeces or from the throat, though it was true that the virus had not been shown definitely to appear in pharyngeal washings. Occasionally epidemics were preceded by upper respiratory infections in the community. One got a picture of contact spread after an incubation period of about thirty days, but whether the spread was by droplet or from faeces could not yet be stated. He was not sure that their methods of epidemiological inquiry at the moment helped them to draw a proper distinction.

Dr. W. H. Bradley said that unfortunately the professional epidemiologist had to spend his time working on notifiable diseases almost exclusively and there was less information about other communicable diseases which had a distinct economic bearing. Here he mentioned "epidemic wry-neck" or fibrositis, and syringe-transmitted jaundice. He hoped the President would tell them whether now, in retrospect, he felt that the type of fibrositis which Beeson and McNair Scott transmitted amongst their colleagues at the Harvard Hospital, Salisbury, during the war, was in fact typical of the disease which was so prevalent in this country that most of us got an attack at some time or other in our lives. He had been privileged to see Beeson and Scott's transmission experiments, and although they did not carry them to the point at which they could demonstrate the actual presence of an agent, he was sure it was significant that they did succeed in transmitting serially through six passages in the human. This seemed to be almost as convincing as anything could be that in the blood of patients there was an agent capable of communicating the ordinary fibrositis seen commonly in this country.

As to syringe-transmitted jaundice, he expected that Dr. Copeman's own experience in rheumatic clinics would have caused him to see a good deal of this in patients receiving gold therapy. Did he feel that there was in this jaundice a factor other than that known as homologous serum jaundice? Did he think it was merely syringe transmission of an agent from patient to patient, or did the gold itself play a part in the production of jaundice in rheumatic clinics where chrysotherapy was practised?

Dr. Maurice Mitman said that he particularly appreciated that part of the President's Address which dealt with the possibility of the infective origin of various myalgias, such as Bornholm disease, epidemic wry-neck, erythema nodosum associated with pain in the joints, and so forth. There had been a tendency to pick out from amongst acute and often chronic joint pains a number of infective conditions which were now fairly clearly defined. Erythema nodosum was an interesting example because, for a long time, it was undecided whether it was a streptococcal disease, a tuberculous condition, a disease *sui generis*, or an allergic disorder. The subject became more complicated when it was discovered that meningococcal septicaemia might have as one of its manifestations erythema nodosum, and that some sulphonamides might produce a similar reaction. Did the

in that community of mild murine typhus, and the infestation of its members with lice. The lice feed upon the murine-infected blood, and after a few "passages" through the louse-man cycle, they appear to take on exanthematic properties and the disease becomes epidemic.

The Naples epidemic broke out simultaneously in all the poorer sections of the city and by March 1944 about 1,500 cases had been notified. The peak was reached in January and a sharp fall in daily incidence occurred in the middle of this month. The factors which were underlying the occurrence of the outbreak were evidently numerous, but Stuart-Harris (1947) lists the refugee conditions prevailing amongst the civilian population, the use of overcrowded air-raid shelters as homes, and the shortage of first-class protein in the dietary. Their public health system had entirely broken down, as had the ordinary sanitary services of the city. Throughout the epidemic the younger age-groups were involved to a greater extent, but the mortality, as is usual, was greater in proportion to age. It was soon realized by the Army hygiene officers that the health of the civilian population in such circumstances was intimately connected with that of their troops with whom it was impossible to prevent more or less intimate contact, and co-operation with civilian practitioners was organized by them. About the middle of December, a scheme for the treatment of contacts by means of D.D.T. (and other insecticides) was put into operation by means of the American "six-shot" method of application by use of a dust-gun. This method does not entail the removal of clothes, and thus very large numbers of cases can be dealt with in a comparatively short time. Towards the end of the month, public dusting stations for this purpose were opened all over the city, and by the end of February 1944 over 2,250,000 people had been dealt with in this way. Much of the credit for this achievement must go to the American Typhus Commission under the energetic leadership of Brigadier-General Fox and assisted by 17 selected officers from the R.A.M.C. Towards the end of March, the epidemic finally petered out. The important lessons which we learnt from this rather dramatic episode are tabulated by Chalke (1946) as follows:

- (a) An epidemic of typhus can be terminated in the winter months even in a city where conditions are most favourable for its spread.
- (b) Intensive searching for cases and the disinfection of contacts and the general public were the most important measures adopted. Other public health measures must not be overlooked—in particular the control of movement.
- (c) An army can live and work in a typhus-ridden city with almost complete impunity, provided discipline is maintained and prophylactic dusting is carried out efficiently and regularly.
- (d) The principle of dusting fully clothed people, using hand or power-dusting apparatus, is a notable advance on former methods of dealing with lousiness in a community. Its use in the Army allows cumbersome steam and hot-air apparatus to be done away with.
- (e) Any efficient insecticide powder applied in this way will be successful in guarding against infestation and reinfestation, as well as in treating it. The method is without equal for dealing quickly with large groups of people. Its worth was proved at a later date in disinfecting immense numbers of prisoners and refugees.
- (f) D.D.T. is a new weapon in preventive medicine. It does not kill lice quickly, but is non-irritant and persistent, having residual action which prevents reinfestation. It is particularly valuable where people are not under strict discipline and washing and laundry arrangements are defective.
- (g) Civilian inoculation was not of much importance in the extinction of the epidemic. The British Army, which escaped with one case, contained a large number of uninoculated troops at the peak stages.

Section of Neurology

President—C. WORSTER-DROUGHT, M.D.

[March 4, 1948]

DISCUSSION ON RUPTURE OF THE INTERVERTEBRAL DISC IN THE CERVICAL REGION

Dr. W. Russell Brain: *Anatomy.*—Disc protrusions are common in the cervical and lumbar regions and rare in the thoracic. The cervical and lumbar regions of the spine both exhibit a secondary lordotic curve which, in the cervical region, is largely contributed by the intervertebral discs. They are both sites of much greater mobility than the thoracic spine, and they are each especially exposed to trauma, the lumbar spine to the stresses and strains imposed by weight-lifting and by falls on the buttocks; the cervical spine to the effects of violent movements of the head. In the cervical spine the intervertebral discs are larger relative to the vertebrae than in the lumbar spine, and they are related to the spinal cord as well as to the nerve roots. The cervical spinal cord is anchored fairly firmly by means of the ligamenta denticulata and the roots run a short and direct course to the intervertebral foramina, the uppermost running slightly upwards, the mid-cervical roots transversely and the lowermost beginning to run slightly downwards.

The posterior longitudinal ligament expands opposite each intervertebral disc but does not reach to the lateral margins of the disc. Its central fibres are the weakest and this probably accounts for the two main sites of disc protrusion. If the central fibres are ruptured the disc protrudes straight backwards in the middle line. If this does not happen, or if the disc protrudes slightly to one side, it extends laterally to emerge at the outer edge of the ligament.

In addition to the anterior and posterior spinal arteries the cord is supplied by the lateral spinal arteries which pass in through the intervertebral foramina and in the cervical region are derived from the vertebral arteries and the ascending cervical branch of the inferior thyroid artery. In the veins the blood flow is upwards and the longitudinal venous plexuses of the spinal cord itself anastomose through the veins of the spinal roots with the internal vertebral venous plexuses lying between the dura mater and the ligaments of the spine and these again communicate through the intervertebral foramina with the external vertebral venous plexuses which lie outside the vertebral column.

No doubt the earliest changes produced by a protruded intervertebral disc are circulatory and these must be important at all stages. The veins with their thin walls and low pressure would naturally be compressed first and since the flow in them is upwards an œdema of the anterior or anterolateral region of the cord at and for some segments below the site of compression would cause symptoms related to these segments. Similarly, œdema would be produced in the spinal roots compressed. Arterial blood supply is likely to suffer late, if at all, but obstruction of the lateral spinal artery at the foramen would tend to cause ischæmia of the lateral region of the cord. The anterior spinal artery might conceivably be compressed by a mid-line protrusion, and in severe cervical spondylitis the vertebral artery and vein may undergo compression in their foramen.

Pathogenesis.—The material upon which this paper is based consists of 10 surgically verified cases from one of which post-mortem material is also available.

These patients were mostly middle-aged or older. 2 were between 30 and 40, 3 between 40 and 50, 2 between 50 and 60 and 3 were over 60. Only 2 had symptoms of the radicular type alone, in the remaining 8 the spinal cord was compressed. This, of course, does not represent the relative frequency of the two clinical pictures, for patients with spinal cord compression are much more likely to be operated upon than those with symptoms of a root lesion alone. In this series trauma was unimportant as a cause and appeared to have been a possible factor in only 2 cases. On the other hand osteo-arthritis was present in the cervical spine in 7 out of 10, and in 1 other, though the neck appeared normal, there was osteo-arthritis in the thoracic spine. The osteo-arthritis may be fairly diffuse or limited to the articulations adjacent to one intervertebral disc. In one patient the protrusion occurred during pregnancy.

While it may not be possible sharply to distinguish traumatic disc protrusion from protrusion associated with chronic osteo-arthritis, since the two may overlap, I believe that at the two extremes there are cases in which the protrusion is primarily traumatic and those in which osteo-arthritis is the main causal factor. In the former group it has been suggested that some congenital weakness of the disc may be present, since the precipitating trauma may be very slight, and that is perhaps supported by the fact that I have seen several patients—one in this series—with sciatica as well.

The patients in whom trauma plays a part in the ætiology appear to be younger than those with osteo-arthritis and to be more likely to develop radicular than spinal cord compression.

President consider that these conditions were allergic, or were just picked specific clinical entities from a group which was very mixed beforehand?

Dr. H. J. Parish thought that until the recent war they had probably overlooked skin sores or wounds as manifestations of diphtheria infection. The historical accounts of Trousseau and others showed that cutaneous diphtheria was formerly a most serious condition. The President had spoken of the infected desert sores seen in Palestine during the war, and many skin lesions were also found in prison camps in the Far East. Bacteriological examination was not carried out in these camps, but several patients developed various paralyses; in retrospect, diphtheria could be diagnosed with confidence. There was no doubt that this type of infection had to be reckoned with from time to time.

Secondly, the President had mentioned the transmission of viruses by injections. The need for good inoculation technique was thus emphasized. A separate syringe and needle should be used for each intravenous injection or withdrawal of blood.

Sir Weldon Dalrymple-Champneys said that they heard much talk nowadays about getting the preventive aspect into the minds of the young practitioner by encouraging physicians and surgeons in teaching hospitals to look at all their cases from a preventive standpoint, and to get their students to do the same. Parallel with that, there was also, as the President had demonstrated that afternoon, the great desirability of getting their students to look at things from the epidemiological point of view. They were all conscious of the fascinating problems waiting to be solved and the important discoveries waiting to be made.

It was curious that whereas it was well recognized in tropical countries that there were one-day fevers and two-day fevers, and so on, most of them were attributed to some virus infection, and most of them were so mild that no one worried about them but took them as one of the ordinary commonplaces of life. In temperate climes they did not seem to have paid much attention to these things. They liked to go on studying well-recognized diseases or more serious diseases, and all these "colds" and "influenzas" were occurring and unless they could find the virus they were being allowed to drift past them. Personally he hoped that in the future more attention would be paid to these matters, and as a result some of the discoveries to which the President had referred would be made.

With regard to epidemic myalgia, he was struck at the time by the fact that some of these cases did become chronic. They were not all trivial things. He would have thought it very probable that many of these "trivial" illnesses included a certain residue of cases which had become chronic and which generally were quite unrecognized except in the hands of the able epidemiologist.

The President said that Dr. Bradley had asked whether he could have told that the cases of fibrositis of Beeson and McNair Scott were not typical ones. Of those he saw he was quite unable to say which of them had become chronic owing to natural causes and which had arisen out of the epidemic. Some became very severe, two of them at least had to be sent back to America as they seemed quite intractable to treatment, and that might indicate some degree of differentiation.

The transmission experiments were interesting. This was also done in a case of rheumatic fever, and again, something happened, that is to say, quite definite "rheumatic" symptoms arose in four generations of inoculation from this case of rheumatic fever. They were unable, however, to carry the matter further at that time.

In reply to Dr. Mitman, his view was that a large group of cases in the whole field of the rheumatic diseases—not only in the non-articular type—still awaited further classification. There was still a large field for purely clinical observation and he felt sure that they would, bit by bit, sort out that field.

With regard to gold-produced jaundice it was very rare in rheumatic clinics, so that he thought it must be considered sporadic rather than homologous, and probably something specifically to do with the gold itself.

Sir Allen Daley said that the advances for which they hoped could come about only with the closest co-operation between the clinician and the professional epidemiologist, if he might use that term. The professional epidemiologist might be able to throw some light on the problems, but he was not sufficiently close to them, and it was the practising physician, the clinician, who, if he had in his bones the elements of epidemiology, could ascertain that there was a problem there. Many clinicians neglected this entirely. Therefore the Section was very fortunate in having as President a man who had done a large amount of clinical work with the Army in the field, and had drawn attention to numerous and most interesting epidemiological studies which had arisen there.

lesion was fairly common. Posterior column sensibility was rarely affected. (d) Fasciculation was occasionally seen in the upper limbs, but muscular wasting was inconspicuous except in the hands where it was several times noted even with a lesion as high as C2 to C3. This may be the result of a circulatory change produced by compression of spinal veins, but if so this region of the cord must be especially vulnerable.

(4) *The cerebrospinal fluid:* The C.S.F. was examined in 9 cases and was abnormal in composition in 7. The protein was between 60 and 80 mg. % in 3 and between 100 and 140 mg. % in 4. Queckenstedt's test yielded evidence of subarachnoid block in 4 in one of whom the composition of the fluid was normal. Thus in 8 out of 9 the investigation of the C.S.F. yielded some abnormality.

(5) *X-ray examination:* X-rays may show no abnormality, or merely a narrowed disc space, but in this series osteo-arthritic changes were present in the neck in 7 out of 10 cases and myelography yielded positive results in all 6 cases in which it was carried out.

(6) *Movements of the neck:* Some limitation of neck movement is often present. In the more acute cases a very slight movement may cause pain: in some cases with chronic osteo-arthritis on the other hand neck movement may be surprisingly full and painless.

Diagnosis.—In patients with radicular symptoms only the main problem in diagnosis is to distinguish a protruded disc from cervical spondylitis with a root lesion due to narrowing of the intervertebral foramen. In both osteo-arthritic changes may be present with loss of disc-space and hence a narrowed foramen. A raised protein in the C.S.F. may occur with a disc protrusion compressing the roots only but not in arthritis. In doubtful cases only myelography will settle the question.

The diagnosis of a protruded disc from other extramedullary tumours can be made only when the characteristic X-ray changes are present in the cervical spine.

Prognosis and treatment.—As with herniated lumbar discs recovery from radicular symptoms may be achieved by conservative measures. Prolonged immobilization with the neck between sandbags or with traction extension or support from a plaster or leather collar should be tried and operation carried out only for persistent pain in the neck or upper limb, or severe muscular wasting and weakness. Spinal compression always calls for surgical exploration.

Mr. G. C. Knight: In the cervical canal the neural structures are relatively immobile and small herniations may therefore produce compression, not only of an adjacent nerve root but also of half, or the whole, of the anterior aspect of the spinal cord.

Each cervical root runs almost transversely across the face of the disc to reach its point of exit, each root crossing only one disc. Compression of two roots by a single protrusion is therefore rare. Evidence of compression of two roots almost invariably means two compressing agents, and these are not necessarily discs.

Although Stookey in his original description divided cases of cervical disc protrusion into three groups, those showing root compression, or root compression with hemi-cord compression, or mid-line compression of the front face of the cord, there is reason to believe that cervical disc protrusion may at times be a progressive lesion: cases passing progressively from root compression alone to root compression with hemiparesis, and finally to paraparesis. The interval elapsing before the development of symptoms of cord compression may be long, as in a case recorded by Michelson and Mixter in which pain in the arm and shoulder preceded by twenty-three years the onset of paraparesis.

Symptomatology of acute traumatic protrusion.—Minor injuries in the cervical region may be followed by the instantaneous development of traumatic paraplegia. Such an injury may be inflicted by a fall down a few stairs, by an elderly patient falling on his face when walking along the pavement, and has followed sudden movement of the neck if a patient is pitched forward by the sudden arrest of a car. X-ray examination in such cases may reveal no evidence of cervical spinal fracture or dislocation. It has been suggested that in cases of this nature dislocation of the spine has occurred but the bones have rebounded into their normal position. Such a state of affairs is impossible owing to interlocking of the articular facets. Certain cases of this type are attributable to cervical cord contusion produced by hyperextension of the spine and rupture of the anterior common ligament, but others are clearly due to a sudden protrusion of a cervical disc, the effect of which will depend upon the degree of contusion inflicted on the cord at the moment of herniation. If the herniation produces a lesion in the anterior spinal artery at the site of impact the case will be irrecoverable; there is an immediate quadriplegia, the level of anaesthesia extends up to the arms, and gradually ascends to a still higher level, as the result of anterior spinal thrombosis which may even produce phrenic palsy within twenty-four hours.

Less serious cases are observed in which the cord escapes severe vascular injury; in these there is a substantial prospect of recovery. There may be an immediate quadriplegia, but the sensory loss extends only to the thorax and tends to pass off quickly. Within a matter

The role of osteo-arthritis in causation is obscure: it is in this group that the protrusion is likely to be osteophytic in part, and possibly some of these swellings are not derived from the disc. In the one case with post-mortem material—a patient with cervical and thoracic spondylitis from whom a left antero-lateral protrusion at the level of C4 to C5 had been removed—three out of four adjacent intervertebral discs in the thoracic region were the site of a cartilaginous nodule. Histological examination showed at the site of the operation the remains of a cartilaginous protrusion beneath a greatly thickened dura fused with the posterior longitudinal ligament, while in the thoracic region there was a degenerated intervertebral disc which had ruptured into the body of one vertebra. In such a case herniation of a disc is clearly only an element in a diffuse degenerative spondylitis. In this series the disc between C5 and C6 was involved five times, that between C4 and C5 twice and C2 and C3, C3 and C4 and C6 and C7 once each.

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The root syndromes are most sharply distinguished by the distribution of the paræsthesiæ. In compression of the sixth cervical nerve root paræsthesia will be felt at the radial side of the forearm and thumb, and in the first interosseous space; in compression of the seventh root paræsthesia will be experienced upon the back of the index, middle and ring fingers and the whole dorsum of the hand. The physical signs consist of local tenderness to palpation of the upper fibres of the trapezius and suprascapular region, and occasionally of the anterior pectoral areas. Usually, lateral flexion of the spine towards the side of the lesion increases pain, but flexion in the opposite direction may also do so, according to the relationship of the root to the protrusion. Long axis compression of the spine, as described by Spurling and Scoville, will not invariably lead to exacerbation of the pain.

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Treatment.—There can be no doubt that the majority of cases of cervical disc protrusion recover spontaneously as a result of conservative measures alone. Rest in the position of

greatest comfort should be tried first. Manipulation is dangerous owing to the risk of increasing a protrusion. Certain successes attributed to manipulation may be accounted for merely by the beneficial effects of the anæsthetic employed, which will relieve muscle spasm. There are no indications for any surgical intervention in the stage of irritation of a single nerve root, which should invariably recover as a result of conservative treatment. Surgical intervention will be needed occasionally in cases of established compression of a root in which conservative treatment has failed, and in all cases of half-cord compression. In syndromes of compression of the front face of the cord by mid-line protrusions there are points for and against operation which must be most carefully weighed. Attempts at removal have occasionally led to an increase rather than a decrease in the neurological signs. In high mid-line protrusions in which signs of defective movement of the diaphragm are already present, even a simple decompression may not be advisable.

In 37 cases under my care there were 29 examples of compression of a single root. 24 were relieved by conservative measures, which included the application of a plaster collar in 4 long-standing cases, after a preliminary period of skull caliper traction in 3 in whom the symptoms had been present for as long as seven years. (Laminectomy was required in 5.) 4 cases exhibiting compression of half the cord required laminectomy. In 4 cases of mid-line protrusion laminectomy with decompression was employed only in 2 owing to unfavourable features that were present in the other cases.

When operation is employed hemilaminectomy gives an adequate approach in cases exhibiting root symptoms only, removing the ligamentum flavum and the lower third of the upper lamina and the upper half of the next lamina below. This bone removal must be carried far laterally. The affected root will be found to be flattened and displaced posteriorly, and is usually extremely tense. It is best to draw the root up and remove the protrusion from its inner aspect, the portion of tissue removed being usually small in size.

A full laminectomy is required in those cases in which symptoms of cord compression are present. In cases of mid-line protrusion it is usually wiser to treat the patient by a simple decompression, with mobilization of the dentate ligaments, rather than risk the possibility of an anterior spinal artery thrombosis with its possible fatal consequences from phrenic palsy being precipitated by dissection and manipulation in contact with the front face of the cord.

Dr. J. W. D. Bull: In studying the question of protruded intervertebral discs it may be helpful to compare and contrast the anatomy of the lower cervical and lower lumbar vertebræ, for it is usually the lower vertebræ in each case which are involved. Taking the lumbar vertebræ first, for here we stand on firmer ground, as far as the ætiology of the disc syndrome is concerned, we find that these are the largest vertebræ in the body and the largest intervertebral discs. Their size, of course, is in keeping with the great pressures they are called upon to withstand. The volume of these discs is about 10 c.c. and if we allow the nucleus pulposus to be 15%—probably a generous estimate—of this volume, that is to say 1.5 c.c., then this is the volume which can potentially protrude. A spherical body of 1.5 c.c. has a diameter of a little over 1.4 cm., or half an inch, or the size of a small cherry. A body of such a size protruding into the lumbar canal will, and does, cause considerable obstruction and occasionally a complete block of the spinal canal. The canal in the lower lumbar region is traversed by the lower lumbar and the sacral nerves running longitudinally—the cauda equina.

In the lower cervical region there is a different anatomical picture. The vertebræ are very much smaller—the surfaces of their bodies have an area about four times less than the lumbar, and their intervertebral discs are correspondingly smaller. I have dissected out the intervertebral discs from the neck of a body whose vertebræ and discs were radiologically normal. The volumes of the discs were determined by placing the dissected fragments in a small test tube graduated in c.c. The measurements were:—C4 to C5 disc 1.0 c.c., C5 to C6 disc 1.2 c.c. and C6 to C7 disc 1.4 c.c.

This is a very much smaller volume, naturally, than the lower lumbar disc. Using the same arbitrary figure, 15%, for the volume of the nucleus pulposus, we find that if the nucleus between C6 and C7 protrudes entirely, a volume of 0.21 c.c. is extruded. Such a body, if spherical, will have a diameter of 0.7 cm., about half the diameter of the lumbar disc, whose volume is seven times greater. Such a protruded cervical disc would be about equivalent in size to a red currant and this, one must remember, is the maximum protrusion. Most protruded cervical and lumbar discs would be smaller than I have described as the extrusion of the nucleus pulposus is not normally complete.

In the lower cervical canal much of the space is occupied by the spinal cord. Here the nerves do not run parallel in the line of the canal as in the lumbar region, but instead leave the cord almost at right angles.

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Fig. 3 is a semi-diagrammatic illustration, intended to show the anatomical changes which occur when a disc degenerates. (A) shows the normal. Attention is drawn to the considerable space between the posterior wall of the disc and the cord. (B) shows a centrally protruding disc. This can and does occasionally occur. If large enough it behaves as an anteriorly situated extradural tumour, and was so regarded by the older surgeons before discs became the fashion.

I cannot believe that a disc *per se* can produce a complete block to the flow of cerebro-spinal fluid, as we sometimes see, but that some degenerative or neoplastic process is super-added: that, in fact, the older surgeons were less inaccurate in calling the lesion a chondroma. (C) illustrates the laterally protruding disc. This is the type generally regarded as producing the so-called cervical disc syndrome, a brachialgia, a pure lower motor neurone lesion.

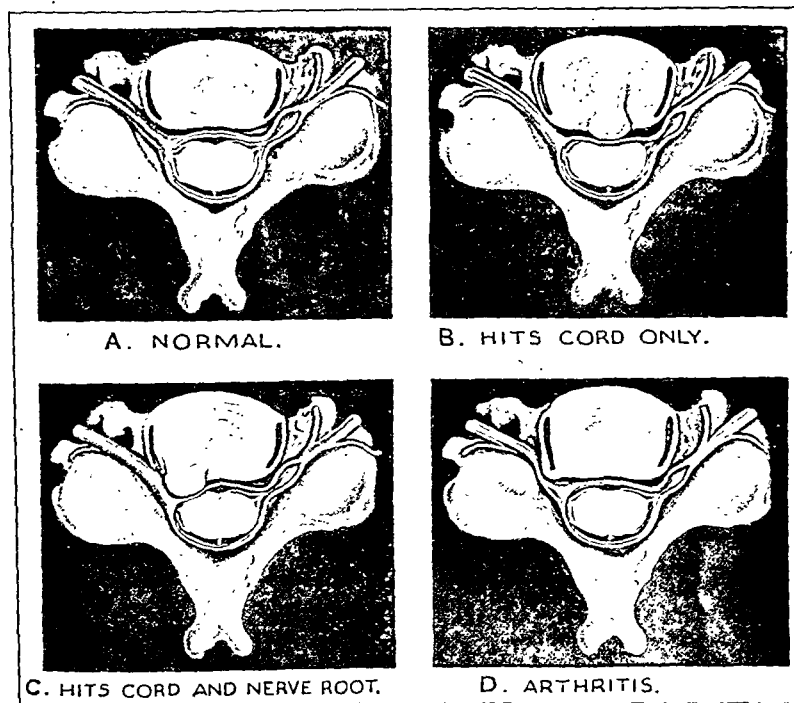


FIG. 3.—Four types of "cervical disc". [Drawing by E. R. Alexander.]

Two things make one feel somewhat sceptical about this morbid anatomical picture. First it must be anatomically difficult for the disc to hit the nerve and miss the cord. Krogdahl and Torgersen (1940) showed how strong were the ligaments of the neuro-central joints. These ligaments must tend to deter the lateral wandering of protruded discs. Secondly, one is profoundly disappointed by the surgical findings. So often one reads an operative description where a laminectomy only was performed and the protruded disc was seen pressing on the nerve. But rarely, it seems, is the disc actually removed.

Lastly, let us consider the nerve as it issues between the two joints I have mentioned (fig. D). Here we must go back to the morbid anatomy for a moment and consider a case which shows narrowing of the C5 to C6 disc space and/or narrowing of the C6 to C7 space. As a result of this narrowing abnormal strain is placed on the joints of Lushka and the articular joints of the pedicles. It is fair to assume that arthritic changes supervene in these joints. The articular cartilages rub one another, a small effusion may collect in the joint, the periarticular tissues thicken and later osteophyte proliferation occurs—in fact all the well-known changes which occur in any joint in such circumstances. When these things occur the issuing nerve has every chance of being compressed, both from in front and from behind, as Krogdahl and Torgersen showed.

The pathological changes in Lushka's joints can be detected radiologically by taking oblique views of the cervical spine. This is a most important projection—far more important than the frontal views. Frequently one can detect the presence of osteophytes.

Radiological technique.—(1) *The straight X-rays:* Four projections should be taken,

Two pairs of joints abut on the issuing pairs of nerves. One joint lies in front, the other behind. In all other regions of the spine except the lowest five cervical vertebrae there is only one pair of joints. The joints of the atlas and axis lie in front of the nerves, and elsewhere—except in the lower cervical region—they lie only behind the nerves. The posteriorly situated joints are well known—those articulating the pedicles of adjacent vertebrae. The anterior joints are less well known and they receive very scant mention, in very small print, in the latest edition of Gray's "Anatomy". They are not even honoured with a name and receive no mention at all in the section on arthrology.

It was Luschka (1858) who first described these joints. He pointed out that the upper and lower surfaces of the bodies of the lower cervical vertebrae are curved at their posterolateral edges. Between each vertebra in this situation are small joints with synovial linings. His description seems not to have been improved upon and it is interesting to note that he regarded the joints as the homologues of the costovertebral joints in the thoracic region—a rather remarkable observation published one year before Darwin's "Origin of Species".

In modern times, Frazer in his "Anatomy of the Human Skeleton" makes certain observations, which I have summarized. "The first two cervical nerves", he said, "differ from all other spinal nerves in that they issue behind the articular masses. The explanation is that the articular masses concerned are morphologically different from those lower down. If the upper surfaces of the bodies of the middle and lower cervical vertebrae are inspected a prominent neurocentral lip is standing up outside the junction of the costal element and

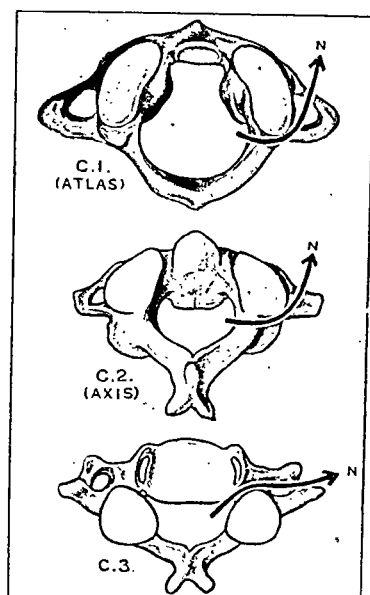


FIG. 1.—N=Nerve.

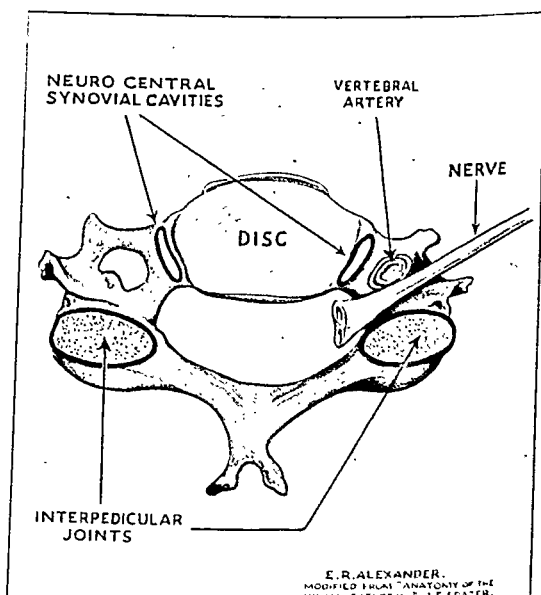


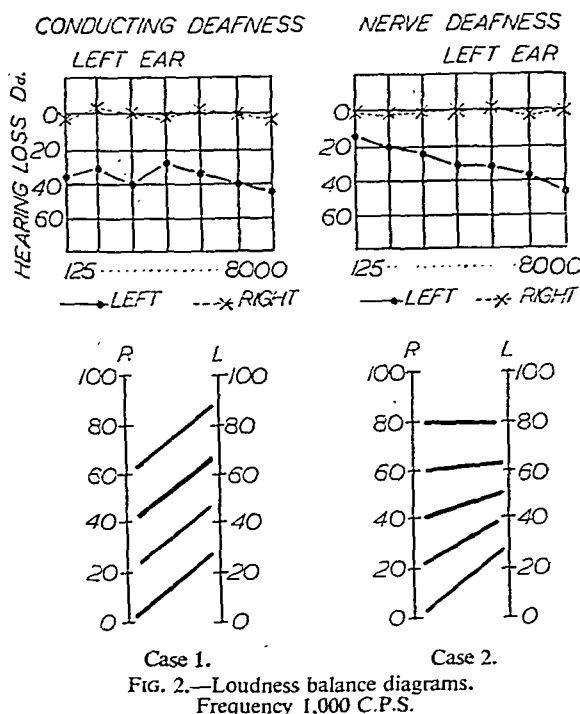
FIG. 2.—Typical cervical vertebra.

the neural arch, with the centrum; in the recent state a small synovial cavity lies between this lip and the bone above, outside and behind the intervertebral disc." Frazer goes on: "From its position this joint cavity is in front of the issuing nerve. These small joint cavities are probably in series with the costovertebral joints in the thoracic region." As I have said Lushka pointed this out nearly hundred years ago (fig. 1, after Frazer).

The lower pairs of cervical nerves are unique in being bounded both anteriorly and posteriorly by a joint as they issue from the spinal canal (fig. 2, after Frazer).

Pathological aspects.—When one X-rays the cervical spine one is struck by the frequency of narrowing of two intervertebral discs—those between C5 and C6 and C6 and C7. One is also struck by the normality of the upper cervical discs and, indeed, by the relative normality of all the other intervertebral discs except the lumbosacral, which is frequently narrow. I think that narrowing of the disc space indicates some degeneration and that the disc is no longer normal. I do not think that we are justified in assuming that it often means a protrusion backwards into the cervical canal, sufficient to cause symptoms.

Those cervical discs even when they protrude to the maximum are tumours no larger than red currants and frequently, of course, they would be much smaller.



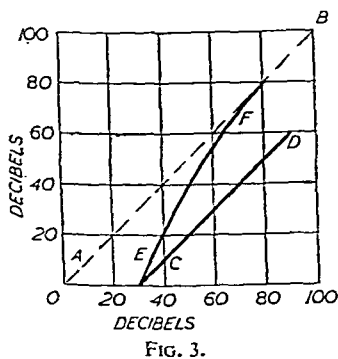
intensity for the left ear will, of course, be 30 db. higher. Successive stimuli, rising in intensity in steps of 20 db., are then applied to the right ear and for each level the balancing intensity for the left ear is established by trial, the comparison being made by switching the stimulus backwards and forwards between the two ears. The result obtained in Case 1 indicates that the loss of sensitivity or deafness of the affected ear, 30 db. at threshold, remains constant at 30 db. throughout the entire intensity range.

This finding is an unvarying one in conducting deafness and is explicable on the straightforward assumption that the obstruction caused by the middle-ear disease to the sound waves on their way to the inner ear introduces an attenuation factor, in this case 30 db., which is constant at all intensities.

A very different result is obtained in Case 2. The audiogram is substantially the same as in Case 1, with a threshold shift at 1,000 cycles of 30 db. The balancing

points at threshold are identical with those of Case 1, with a 30 db. displacement upwards for the left ear. On ascending the intensity scale, however, it is found that the sensitivity loss or deafness of the left ear, 30 db. at threshold, becomes progressively less, until at 80 db. equal intensities at the two ears evoke equal loudness responses. In other words, the deafness of the affected ear present at threshold disappears at higher intensities, and this in its simplest terms constitutes the phenomenon of Loudness Recruitment.

A more conventional form for the graphic representation of these results is that given in fig. 3.



Sound intensities in decibels above the normal threshold are plotted on the vertical axis for the unaffected ear, and on the horizontal axis for the deaf ear. Equal loudness levels for the two ears are plotted on these charts as a series of points and the line AB passing through the origin connects the points which would be thus obtained in a normal individual.

CD is the corresponding line obtained in Case 1. Here the sensitivity loss at threshold of the deaf ear is represented by the displacement of the point C along the base line to the right of the origin. This sensitivity loss remains constant at higher intensities, and the line CD thus lies parallel to AB.

EF is the corresponding line obtained in Case 2. As in Case 1 the same sensitivity loss at threshold is represented by the same displacement of the point E to the right of the origin. At high intensities, however, this sensitivity loss is progressively eliminated, and the line EF approaches and finally coincides with the line AB.

There is general agreement by all who have since investigated the L.R. phenomenon that it is absent in deafness due to uncomplicated middle-ear disease, so-called conductive deafness.

On the other hand, it has frequently been demonstrated in a wide variety of disorders of the internal ear and cochlear nerve, including Menière's disease, which are collectively described as "nerve deafness", and it has come, therefore, to be regarded in a somewhat uncertain manner as a valuable indication of "nerve deafness" using the term in its widest sense.

anteroposterior, true lateral and right and left obliques. Each of these may be taken on 8½-in. by 6½-in. films. A Potter-Bucky or Lysholm fixed grid should be used for all projections, otherwise the pictures will not be of good quality. It is desirable to take all but the frontal picture with the patient standing or sitting, so that the shoulders may drop to the maximum.

The frontal picture should be taken last when one has examined the lateral view. One can then judge how much the central ray must be tilted in order that it passes along the plane of the intervertebral discs of the last three cervical vertebrae. These discs slope forwards and downwards quite considerably.

If the straight X-rays are normal, then a cervical disc is not present and there is no arthritis of the small joints.

If there is a diminution in the intervertebral disc spaces—and this is common from middle age onwards in the lowest three cervical vertebrae—the radiological conclusions are more difficult. The presence of arthritis of the small joints, even with considerable osteophyte proliferation invading the exit foramen, does not necessarily mean pressure on the nerve. Conversely, the absence of osteophytes does not rule out pressure on the nerve, for the periarticular tissues may be swollen and be pressing on the nerve but they may not cast a shadow on the X-ray film.

(2) *Myelography*. Owing to shortage of space this section of Dr. Bull's paper is omitted.

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[May 6, 1948]

Observations Upon the Loudness Recruitment Phenomenon, with Especial Reference to the Differential Diagnosis of Disorders of the Internal Ear and VIII Nerve

By M. R. DIX, C. S. HALLPIKE and J. D. HOOD

(From the Otological Research Unit, Medical Research Council,
 The National Hospital, Queen Square, London)

Introduction.—The Loudness Recruitment (L.R.) phenomenon was first described in 1936 by E. P. Fowler of New York (1936), and its occurrence in certain varieties of nerve deafness has since been abundantly confirmed (Steinberg and Gardner, 1937; Huizing, 1942; de Bruine-Altes, 1946). The phenomenon can be demonstrated most readily when the deafness is limited to one ear, and the nature of the phenomenon itself can perhaps be best appreciated from the following brief description of the simple test procedure needed for its investigation in cases of this kind.

Fig. 1 shows the test procedure being applied:

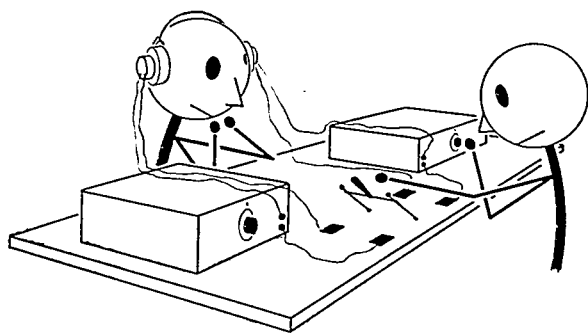


FIG. 1.

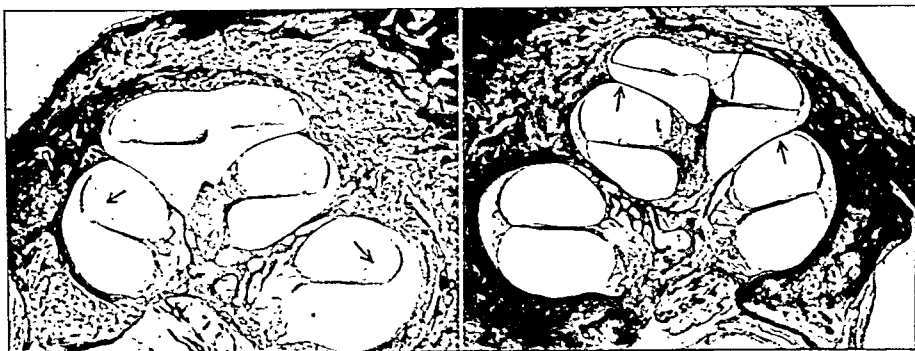
mechanism of the left middle ear, and in Case 2 to Menière's disease affecting the left labyrinth.

The purpose of the test is to ascertain and mark upon the two ladder diagrams two series of intensity levels, one for the right ear and one for the left, each intensity level for the right ear being connected across the diagram with a level for the left ear, found by experiment to give a sensation of equal loudness. In each case the test frequency selected is 1,000 cycles, at which point the audiogram shows a threshold shift for the affected ear of 30 db. The test starts with a stimulus of threshold intensity at the right ear; the balancing

The subject wears a pair of telephone receivers, each supplied by a separate pure-tone audiometer, or preferably by a single audiometer with arrangements for independent adjustment of the intensity in the two receivers. The frequency of the sound stimulus is the same in each receiver, and the tester switches it alternately from right to left.

The audiograms of two typical cases of unilateral deafness are shown in fig. 2.

In Case 1 the deafness is due to a lesion of the conducting

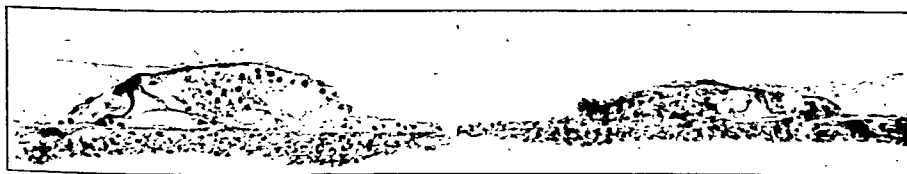
FIG. 4A.— $\times 7.5$.FIG. 4B.— $\times 7.5$.

fairly well preserved, and presents a normal appearance. The cell outlines are well demarcated, and the cell nuclei are clearly differentiated.

It should be noted, however, that as usual in preparations of the human cochlea the technical difficulties of fixation make it impossible to discern any details of the hair cells.

In the affected ear, fig. 5B, marked changes are to be seen in Corti's organ. The cell mass is compressed, the cell outlines obscured and the staining differentiation between nuclei and cytoplasm virtually extinguished.

This type of pathological change in the cochlea was first described by Hallpike and

FIG. 5A.— $\times 200$.FIG. 5B.— $\times 200$.

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Cairns (1938) in two clinically characteristic cases of Menière's disease. Since then, histological studies have been possible in three further cases, in one instance in collaboration with A. J. Wright (1940), and in a second with T. E. Cawthorne (1947).

The findings in a third case have not yet been published.

In addition to these, a number of other histological examinations have been carried out elsewhere (Rollin, 1940; Lindsay, 1942; Altmann and Fowler, 1943) in a number of subjects presenting the characteristic clinical features of Menière's disease.

Whilst in all of these the presence of an endolymphatic dilatation has been established, reports have varied on the condition of Corti's organ. In two of our own series it has appeared normal, and this has also been the finding in the majority of cases reported upon elsewhere. In no less than 3 of our 5 cases, however, Corti's organ has presented abnormalities of the type described. These abnormalities are so striking in character that it would appear inevitable that they should be regarded as being distinctive of Menière's disease in certain of its phases. That they are found sometimes and not always only means, as we see it, that they represent a transient and reversible reaction on the part of the hair cells to the chemico-physical disturbance which goes with the gross distension of the endolymph system. It seems quite reasonable that this disturbance should be phasic in character, so matching the clinical course of the disease, and it is natural, too, that the morphological changes in the hair cells should vary at the same time. It follows, that whether these changes are revealed in any given case or not must be largely a matter of chance, depending upon the phase of the disease at the time of death.

Although these morphological changes may be largely reversible, and may in fact appear to be absent at death, it does not follow that a corresponding reversal need be expected of the functional loss, and, indeed, the fact that the deafness in Menière's disease persists between its active phases can only be taken to mean that while the disorder of structure is apparently reversible, the disorder of function is *not*. The statement that the structural

The theoretical basis of the L.R. phenomenon has been discussed by Lorente de Nó and by Fowler (1939). Both adopt an explanation based upon certain general principles of neurophysiology and upon certain details of the finer structure of the cochlear neurones described earlier by the former. According to this explanation—a somewhat complex one—the occurrence of the phenomenon might be expected as a natural consequence of any pathological process involving a reduction in numbers of the neural elements, either of Corti's organ or of the cochlear nerve, and the matter is put by Lorente de Nó (1937) in the following terms:

"If a number of hair cells in the ear or a number of fibres in the cochlear nerve is missing, the tones will appear to be weaker in intensity when near threshold stimuli are used; but if the intensity of the tone is increased, the more strongly activated hair cells or cochlear fibres will be sufficient to saturate, i.e. to excite with the limiting intensity the cochlear fibre or the cells of the cochlear nuclei, so that the cerebral cortex will receive the same number of impulses per second from both ears and will perceive the tone delivered to the diseased ear as strongly as the tone delivered to the normal or less affected ear.

"Thus, it may be said that Fowler's phenomenon is an immediate consequence of the anatomy and physiology of the nervous system, and that, in fact, it must be pathognomonic of neural deafness".

The phenomenon of recruitment, or the variable type of deafness as they call it, is also discussed by Stevens and Davis (1938). These authors, too, accept the view that the phenomenon is attributable to "a deficiency in the total number of neural elements which normally contribute to give a tone loudness".

It must be said of the explanation that its implications are not devoid of obscurity. Moreover, in some of the cases in which the phenomenon has been found to occur, we seriously lack secure information on the nature of the pathological process. It has, therefore, been clear for some time that the confirmation of de Nó's explanation, and indeed any further developments of theory, must await a great deal of additional factual information. de Bruine-Altes (1946), in her recent monograph, has stressed very pertinently the particular need for further studies in which the results of L.R. phenomenon tests are more closely correlated with more exact information upon the underlying anatomical changes in the cochlea and cochlear neural pathways.

In the present study, therefore, we have endeavoured to throw more light upon the mechanism of the L.R. phenomenon by means of a detailed clinical study, including full investigation of the phenomenon in a number of patients referred to us by our colleagues at Queen Square and elsewhere suffering from two different and clearly defined varieties of hearing disorder, of which our knowledge both of the clinical features and morbid anatomy can now be regarded as considerable. The two disorders are Menière's disease and degeneration of the VIII nerve due to neurofibroma of the nerve and to other space-occupying lesions of the cerebello-pontine angle.

It was considered that the choice of these two disorders was likely to be particularly illuminating since in the one, Menière's disease, the primary lesion we now know to affect the endolymph system of the cochlea with its contained cochlear end-organs, while in the other, the primary lesion is of the cochlear nerve fibres within the internal auditory meatus. Some further details may be given at this point of these anatomical changes and their correlated symptomatology.

Menière's disease.—Fig. 4 shows the histological condition of the cochleæ in a case of Menière's disease.

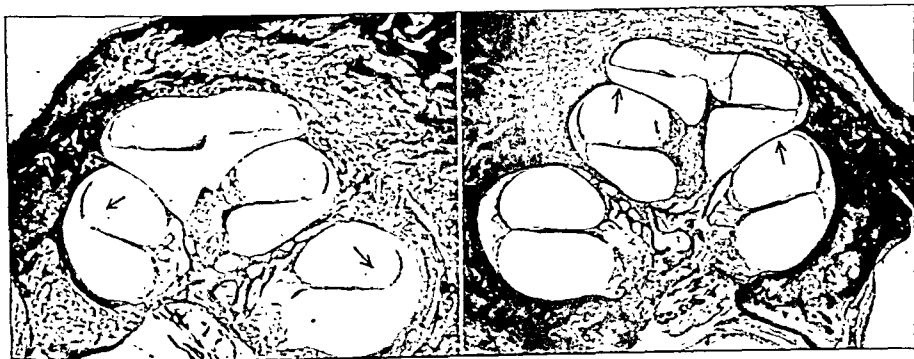
The subject, a man of 46, had suffered for four years from paroxysmal attacks of vertigo with deafness and tinnitus of the right ear. Otological examination revealed a severe perceptive deafness on the right side, and a defect in the right caloric responses. The tympanic membranes were normal and there were no other abnormalities in the central nervous system. The patient died of acute lymphatic leukaemia.

Fig. 4A shows the cochlea of the unaffected ear (left) and fig. 4B the cochlea of the affected ear (right).

In fig. 4A, the normal position of Reissner's membrane will be noted (arrows). Corti's organ appears normal.

The apparent disappearance of Reissner's membrane in fig. 4B has been brought about by the maximal distension of the scala media, which has thrust the membrane back upon the bony wall of the scala vestibuli and caused its herniation through the helicotrema. Arrows indicate the new position of the membrane. It should be noted, however, that the cells of the spiral ganglion appear quite normal in number and structure. Further, there is no apparent reduction in number of the cochlear nerve fibres in the modiolus, or in the osseous spiral lamina.

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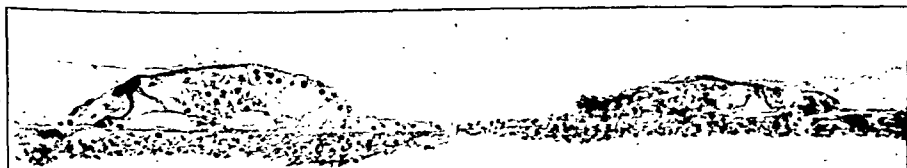
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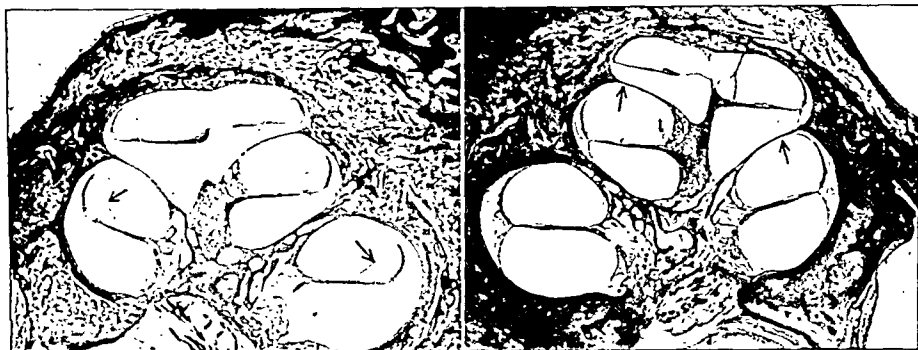
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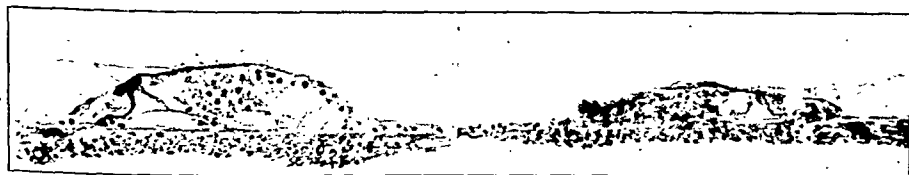
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disorder in Menière's disease is *apparently* reversible requires some amplification in view of the well-known technical difficulties which beset the histological study of the human organ of Corti. Its post-mortem disintegration is rapid, and fixation difficult, and the resulting histological picture is, therefore, always an imperfect representation of the original.

This point will be made clearer from an examination of fig. 6 and its comparison with fig. 5A. Fig. 6 shows the organ of Corti in a cat, well fixed by an *intra-vitam* injection technique. Every detail of the hair cells and their associated membranes is well shown.

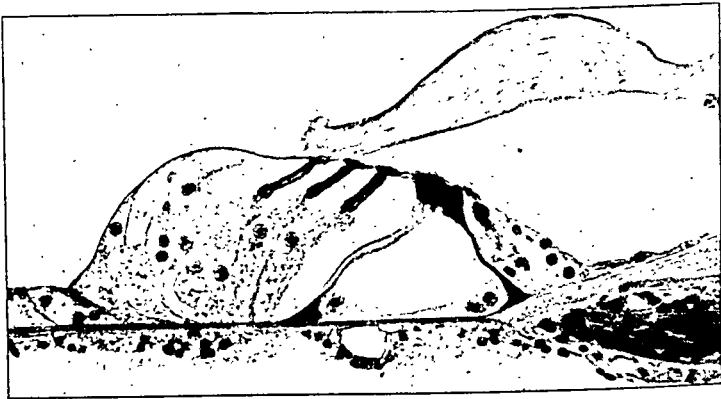


FIG. 6.— $\times 310$.

(Reproduced from Schafer's "Essentials of Histology" by permission of Messrs. Longmans, Green & Co.)

In human material, however, of which fig. 5A is a good representative sample, nothing like this degree of preservation is possible. The hair cells are seldom well defined, and such features as the nerve fibres crossing the tunnel of Corti are never to be seen. This means, inevitably, that changes in the human hair cells, morphologically slight but functionally vital, which are likely to be responsible for the deafness during the negative phases of Menière's disease, will never be demonstrable by histological means.

For this reason, although no definite abnormalities can be recognized in Corti's organ in some cases of Menière's disease, we feel it to be very likely that such changes *are* present and obscured only by the limitations of histological technique.

To sum up the structural changes found in Menière's disease, we can say that these are limited to Corti's organ, but the nerve fibres and cells of the spiral ganglion are normal.

Degeneration of the VIII nerve due to neurofibroma, &c.—Interruption of the cochlear nerve fibres central to the spiral ganglion, whether caused by pressure from a tumour or by surgical section, leads, in contravention of the Wallerian law, to degeneration of the nerve fibres and ganglion cells peripheral to the point of interruption (Witmaack, 1911; Kaida, 1931; Hallpike and Rawdon-Smith, 1934).

Fig. 7 shows a horizontal section through the cochlea of a patient with a high degree of



FIG. 7.— $\times 11$

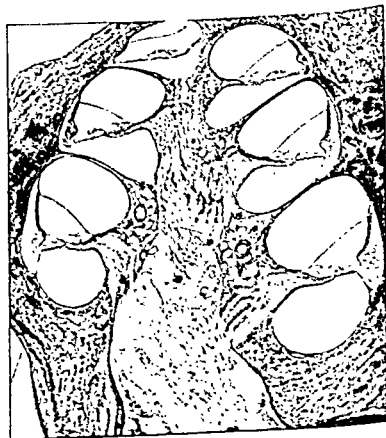


FIG. 8.— $\times 9$.

deafness and a complete loss of the caloric responses resulting from a neurofibroma of the VIII nerve. The tumour is seen filling the meatus, and the fibres of the VIII nerve are lost to view. The main peripheral effect of this tumour is a gross reduction in the number of nerve fibres themselves and of the cells of the spiral ganglion.

Indeed, very few cells of the ganglion remain while the nerve canal of the osseous spiral lamina is virtually empty.

Corti's organ, however, is substantially normal and this is characteristically the case unless the tumour has involved the cochlear blood supply. These cochlear changes in VIII nerve tumours closely resemble in their essentials those which follow an operative section of any mammalian VIII nerve. Fig. 8 shows the cochlea of a cat twelve weeks after an intracranial section of the VIII nerve. It shows again the characteristic disturbance of the whole peripheral cochlear neurone with perfect preservation of the hair cells of Corti's organ. Figs. 9A and B show Corti's organ in these two conditions, namely: Fig. 9A, Neurofibroma of the human VIII nerve; fig. 9B, Degeneration following intracranial section of the VIII nerve of the cat.



FIG. 9A. $\times 200$.—Neurofibroma of the human VIII nerve.

FIG. 9B. $\times 50$.—Degeneration following intracranial section of the VIII nerve of the cat.

This evidence of animal pathology is particularly useful since it indicates that in the human subject there is no reason for supposing that an interruption in the course of the VIII nerve by a tumour would cause any structural changes in Corti's organ, even of a kind which would be obscured by defects of histological technique. The difference in the anatomical findings in the cochlea in these two conditions, Menière's disease and VIII nerve neurofibroma, may thus be summarized as follows:

	Organ of Corti	Nerve fibres and cells of spiral ganglion
<i>Menière's disease</i>	May show gross compression of cells and loss of staining reactions. These changes are not always found. Residual changes, however, are likely to be present and account for the deafness. They are obscured by limitations of histological technique	Normal in number and structure
<i>Degeneration of VIII nerve due to tumour pressure</i>	Normal, unless cochlear blood supply is interfered with	Much reduced in number and may be completely eliminated

The results of the Loudness Recruitment tests obtained in these two groups of cases will now be described.

RESULTS OF LOUDNESS RECRUITMENT TESTS IN MENIÈRE'S DISEASE AND VIII NERVE DEGENERATION

(1) *Menière's disease*.—The number of cases examined was 30. All gave a characteristic history of paroxysmal vertigo, deafness and tinnitus. In the great majority the deafness was substantially limited to one ear, and in all the pattern of the caloric reactions revealed one of the various characteristic abnormalities upon the side of the deaf ear (Cawthorne, Fitzgerald and Hallpike, 1942). None gave any history of head injury, and general neurological examination revealed no abnormalities apart from the octavus system.

In all of the 30 cases, Loudness Recruitment was marked.

Fig. 10 shows the Loudness Recruitment patterns of 3 representative cases with their audiograms. It will be seen that in every one the sensitivity loss at threshold of the affected ear is completely eliminated at higher intensities. In the third case, well-marked over-recruitment is seen; that is to say, at high intensities the loudness function of the affected ear exceeds that of the normal ear. Tests at other frequencies than 1,000 cycles yielded comparable results.

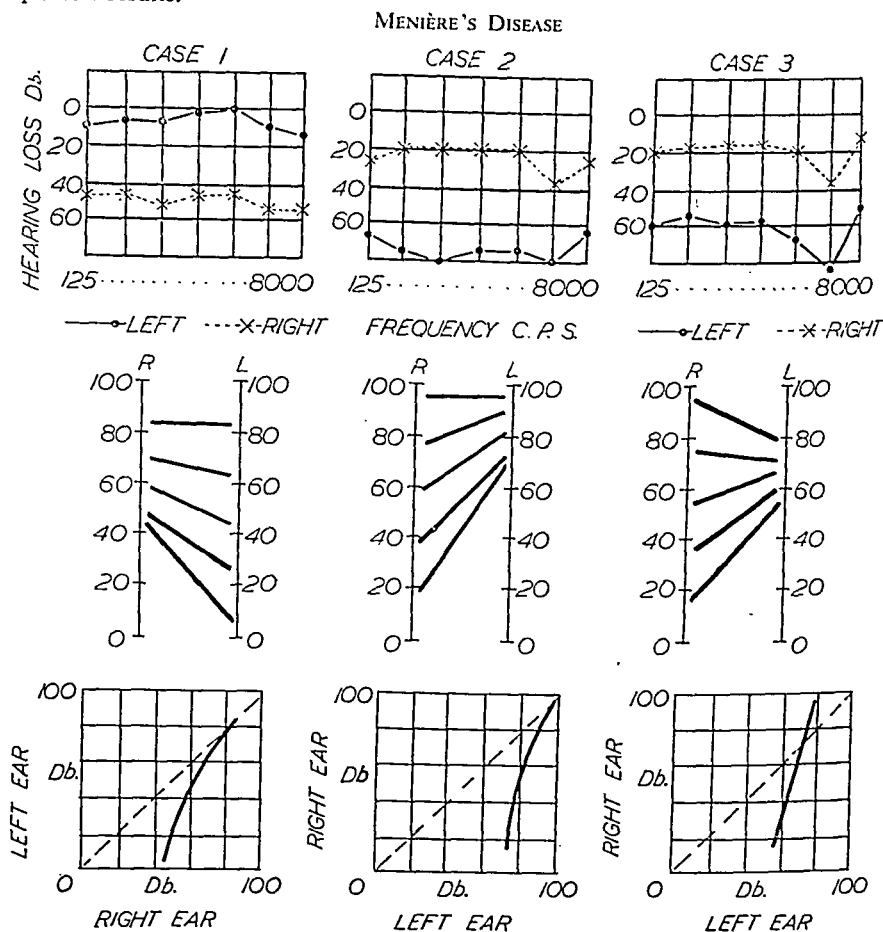


FIG. 10.—Loudness balance diagrams. Frequency 1,000 C.P.S.

(2) *VIII nerve degeneration.*—11 cases of neurofibroma of the VIII nerve were studied, in all of which the clinical diagnosis was confirmed by operative or post-mortem findings. In addition, 9 cases were examined of other varieties of cerebello-pontine angle lesion exhibiting well-marked involvement of VIII nerve function. In 6 of these cases the diagnosis was confirmed by operative or post-mortem findings. It is necessary to stress here that loudness balance tests for the Loudness Recruitment phenomenon can only be carried out satisfactorily when the deafness of the affected ear is of moderate degree. Very often, however, the deafness in cases of VIII nerve neurofibroma and cerebello-pontine angle tumour is severe and not infrequently complete. It has, therefore, been a matter of considerable difficulty to find cases in which the deafness of the affected ear was not too severe for the test. That we were able to find the cases, we owe to the good offices of a number of our colleagues both at Queen Square and elsewhere who have kindly referred their cases to us, and to whom we are greatly indebted.

In the majority of these 20 cases, tuning fork tests showed the typical findings of nerve deafness, reduced bone conduction with a positive Rinne. Bone conduction was, in fact, reduced in all, but in a few the Rinne test was definitely negative in spite of careful masking of the opposite ear.

The results of the loudness balance tests in 14 cases of this group were constant in showing a complete absence of recruitment.

Fig. 11 shows the test results in 3 characteristic cases, together with their audiograms.

VIII NERVE DEGENERATION

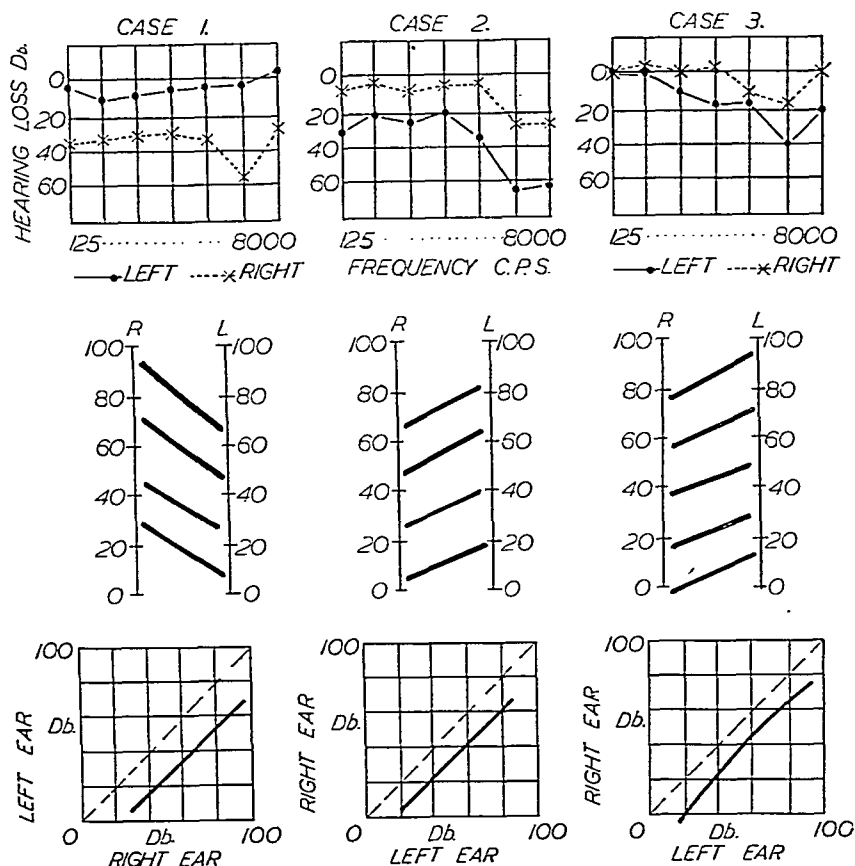


FIG. 11.—Loudness balance diagrams. Frequency 1,000 C.P.S.

It will be seen that in all 3 the sensitivity loss of the affected ear at threshold is maintained at all intensity levels. In the remaining 6 cases of this group a slight amount of recruitment was present. In some of these there was found a fixed upper loudness limit in the affected ear. That is to say, loudness appeared to increase in the affected ear up to a certain intensity level, and thereafter to increase no more. This phenomenon is shown in the second case of fig. 12. Tests at other frequencies than 1,000 cycles yielded comparable results.

SUMMARY OF EXPERIMENTAL FINDINGS

Loudness Recruitment was present and complete in all of 30 cases of Menière's disease, a primary affection of Corti's organ. In 20 cases of degeneration of the VIII nerve, due to pressure or infiltration by tumours, Loudness Recruitment was completely absent in 14. In the remaining 6 cases slight recruitment was present.

It would appear, therefore, that in this condition, an example par excellence of nerve deafness, Loudness Recruitment hitherto described as being uniquely distinctive of nerve deafness is characteristically not present at all. Instead, we have a type of response which is identical with that found in middle-ear deafness.

DISCUSSION

From the viewpoint of practical oto-neurology, the experimental results described make it clear that in the loudness balance test we have at our disposal a test procedure which should prove of great value in making clear the difficult and important distinction between end-organ deafness and nerve-fibre deafness. It seems likely, too, that the findings will prove to have a bearing upon a number of problems of auditory theory. The finding that the recruitment phenomenon is an unvarying occurrence in Menière's disease, a disorder

Fig. 10 shows the Loudness Recruitment patterns of 3 representative cases with their audiograms. It will be seen that in every one the sensitivity loss at threshold of the affected ear is completely eliminated at higher intensities. In the third case, well-marked over-recruitment is seen; that is to say, at high intensities the loudness function of the affected ear exceeds that of the normal ear. Tests at other frequencies than 1,000 cycles yielded comparable results.

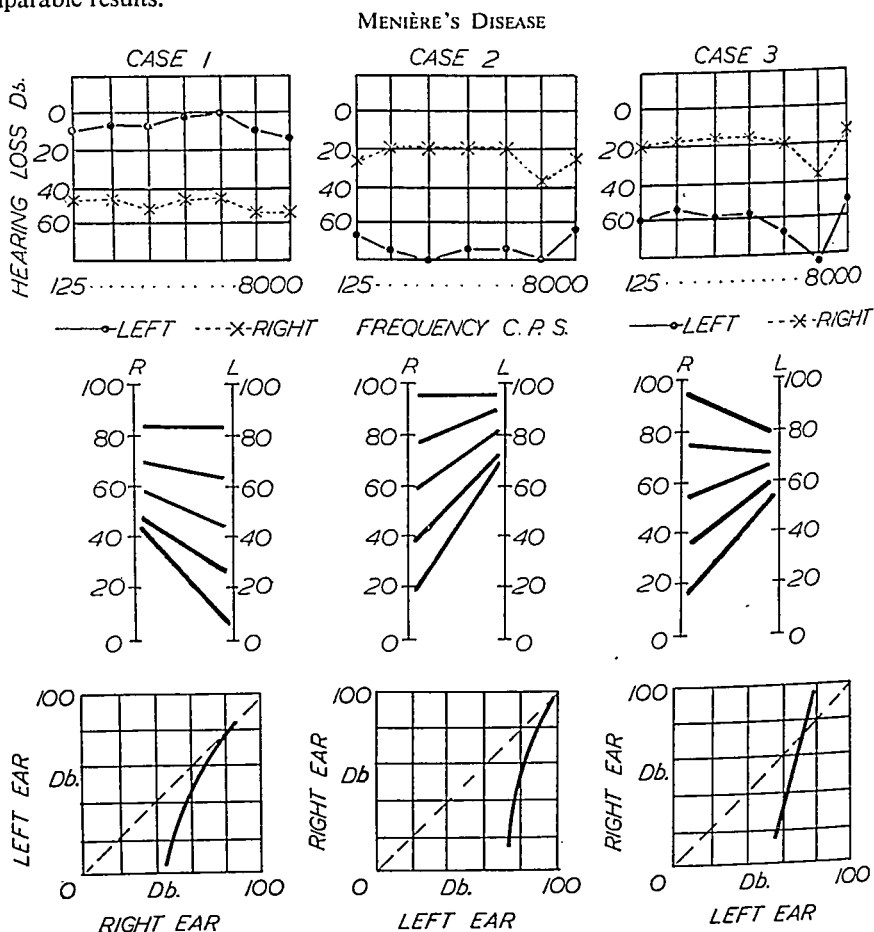


FIG. 10.—Loudness balance diagrams. Frequency 1,000 C.P.S.

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In the majority of these 20 cases, tuning fork tests showed the typical findings of nerve deafness, reduced bone conduction with a positive Rinne. Bone conduction was, in fact, reduced in all, but in a few the Rinne test was definitely negative in spite of careful masking of the opposite ear.

The results of the loudness balance tests in 14 cases of this group were constant in showing a complete absence of recruitment.

Such a formula may be outlined as follows:

The intensity range on the scale shown in fig. 13 lies between four and five bels above the threshold of hearing for a tone of 1,000 cycles, that is to say, it covers the middle range of audible intensity for this frequency, and the total intensity change of 1 bel between the top and bottom of the scale is a tenfold one. Between these points there are twenty just distinguishable increments of loudness, each corresponding to an intensity increment of about 13%, this being the so-called Weber fraction, and according to the data of Shower and Biddulph (1931) the value of this fraction for frequencies between 1,000 and 4,000 cycles approximates very closely to the value given, i.e. 13% for a great part of the loudness scale.

Concerning the manner in which the steps on this loudness scale are related to the number of active nerve fibres, no precise quantitative details are known. We have, however, available a variety of well-known data derived from the electro-physiological recording of cochlear action potentials and from experiments on masking and auditory fatigue, which all indicate that as stimulus intensity is increased there occurs a spatial spread within the cochlea, with progressive activation of additional nerve fibres.

It is suggested that our present experimental finding, i.e. that Loudness Recruitment is absent in diffuse degeneration of the VIII nerve, would be adequately explained upon the following simple hypothesis: That each step on the loudness scale shown in fig. 13 corresponds to a definite fractional increase in the number of activated cochlear nerve fibres. The manner in which this hypothesis might be applied to the working of the normal and degenerate cochlear nerves is shown schematically in fig. 14.

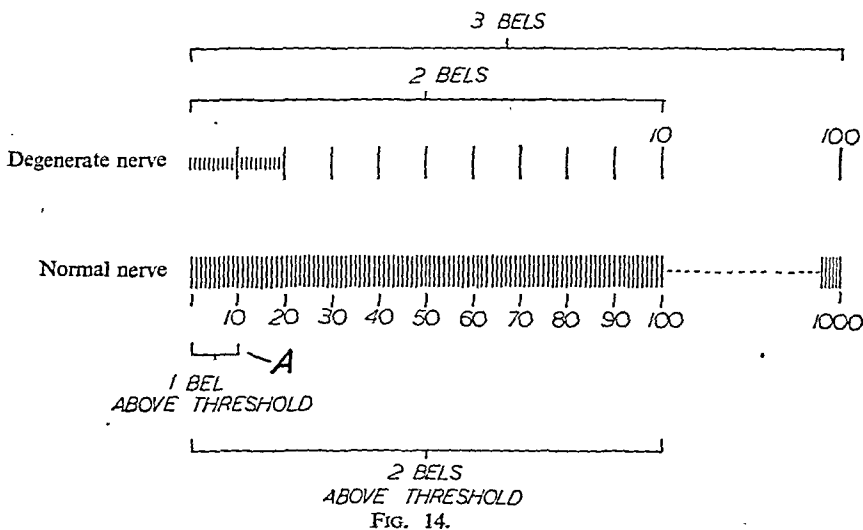


FIG. 14.

This represents the fibres of two cochlear nerves arranged in linear fashion as they lie in the osseous spiral lamina of the cochlea.

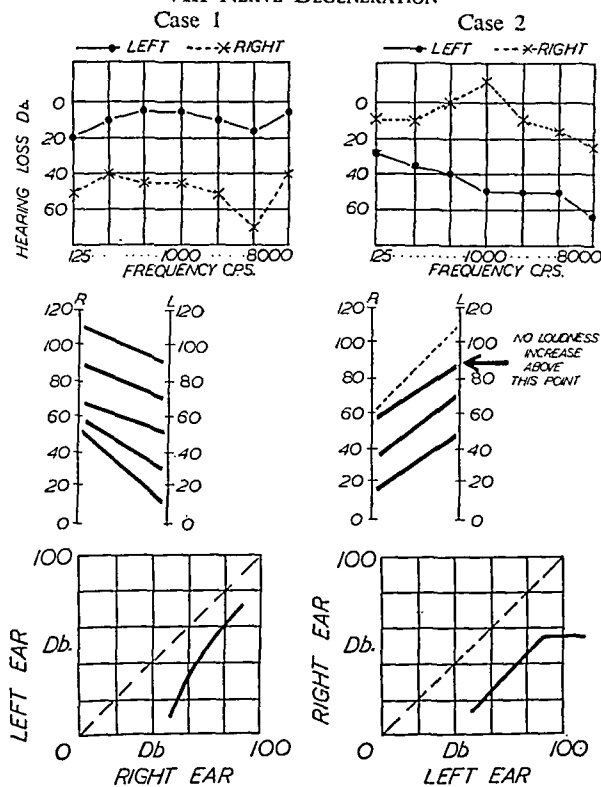
The lower set of fibres is that of a normal nerve, while the upper set is that of a degenerate nerve. The degeneration is diffuse, and the long strokes indicate the surviving fibres. The survival rate is one in ten. The small bracket "A" is taken to indicate the number of fibres stimulated by a sound stimulus of intensity 1 bel above threshold. The number of fibres is conveniently taken as ten. This stimulus exceeds by tenfold the threshold intensity. Correspondingly, stimulus intensities of two and three bels exceed it by one hundred- and one thousand-fold. Now, it is supposed that such changes of stimulus intensity involve corresponding changes in the number of active nerve fibres. This means, in the case of the normal nerve, that the 2 bel stimulus will activate 100 fibres and the 3 bel stimulus 1,000 fibres.

It will be noted that the loudness sensation elicited in the normal nerve by the 1 bel stimulus arises from 10 fibres, and to match this sensation in the degenerate nerve, 10 active fibres will also be required. It is clear that with a fibre survival rate of one in ten, a 2 bel stimulus will be required to bring these into action. In other words, a tenfold intensity increment, 1 bel, is required to compensate for this particular degree of nerve degeneration.

With a stimulus intensity of 2 bels, it will be seen that 100 fibres are activated in the normal nerve. To activate the same number in the degenerate nerve, we require again a tenfold increase of stimulus intensity, i.e. a 3 bel stimulus, and it follows that the same rule will apply as we go further up the intensity scale. In other words, given a constant fibre survival

of the end-organ of hearing, appears to be related in an interesting way to the recent experimental work of Pumphrey and Gold (1948). According to Gold's theory, based upon this work, the microphonic potentials of the cochlea arise somewhere in Corti's organ and play a vital part in determining both its sensitivity and frequency selectivity. We should, therefore, certainly expect that a disorder of this microphonic mechanism, i.e. Corti's organ, would lead to deafness and to certain disorders of pitch sense, i.e. paracusis dysharmonica, well known to be characteristic of Menière's disease. It is pertinent to recall that the very nature of the recruitment phenomenon corresponds very well with a type of derangement well known in certain microphones. Thus a carbon microphone in good order yields an electric response which is linear over a wide range of sound pressures. In a faulty microphone of this kind, however, the response at low sound pressures may be very defective, while approximating at high pressures to something nearer its normal value. It is clear that this variety of non-linearity in the response of a faulty microphone reproduces in essentials the characteristic of the Loudness Recruitment phenomenon, and it seems possible, therefore, that Gold's theory of the cochlear mechanism may provide us with a clearer explanation than any at present available of the occurrence of the Loudness Recruitment phenomenon in Menière's disease.

VIII NERVE DEGENERATION



Showing slight recruitment at frequency 1,000 C.P.S.

Showing loudness saturation at frequency 4,000 C.P.S.

FIG. 12.—Loudness balance diagrams.

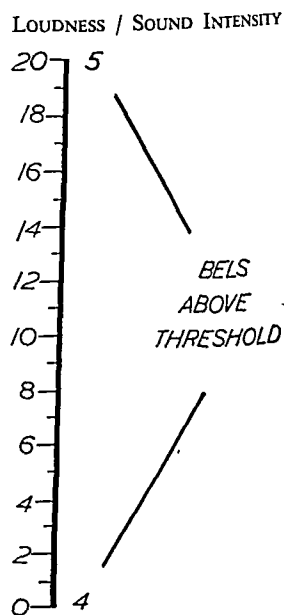


FIG. 13.—Distinguishable loudness steps (each step corresponds to an intensity increase of about 13%).

The finding that recruitment is characteristically absent in cases of VIII nerve tumour has been a very surprising one. Clearly it controverts decisively the theory of its neurological mechanism advanced by Lorente de Nó and Fowler. It would seem quite possible, however, to explain this finding in a different and more simple way if the following assumptions be made: first, that the nerve degeneration engendered by tumour pressure or infiltration is an evenly diffused one with a definite fibre survival rate; secondly, that the relationship between stimulus intensity and loudness sensation depends upon a simple type of formula governing the numerical increase of active cochlear nerve fibres which accompanies each ascending step of the loudness scale.

Section of Dermatology

President—J. E. M. WIGLEY, F.R.C.P.

[March 18, 1948]

Polyarthrititis with Dermatitis. ? Keratoderma Blennorrhagica (Dr. PHILIP ELLMAN'S Case).—DAVID WEITZMAN, M.D., M.R.C.P. (for J. E. M. WIGLEY, F.R.C.P.).

Male, aged 42, complains of an eruption of the groins and feet since October 1947, and of painful swollen joints since November 1947. No urethral discharge.

Past history.—1943: Similar attack of arthritis with a rash in his groins, which subsided after a month's bed rest.

1928: Gonorrhœa, followed by corneal ulcer and transient polyarthrititis.

On examination.—Thin, toxic, febrile. Rheumatoid arthritis of knees, ankles and shoulders. Raised scaly erythematous area round pubes and groins; scattered smaller lesions, mostly regressing, on arms and trunk; ulcerated and crusted areas on toes; thin brittle nails.

Investigations.—Gonococcal complement-fixation test positive (on two occasions). Wassermann and Kahn negative. Skin scrapings; No fungus; culture grew staphylococci and *B. proteus*. Joint fluid: Many pus cells; sterile on culture. Urine: Pus cells; coliform bacilli on culture. Blood picture: Moderate anæmia; white count within normal limits.

Treatment.—Five million units of penicillin and 60 grammes of sulphamezathine.

Progress.—Improvement in the small patches on the arms and trunk, but the lesions in the pubic area and on the feet are unchanged.

Dr. Weitzman added: Dr. Ellman regards the joint picture as typical rheumatoid arthritis, and not gonococcal arthritis. He thinks that Reiter's disease might be considered. I understand from Dr. Wigley that cases of keratoderma have recently been reported to have cleared up after intensive penicillin therapy.

Professor Ö. N. Holsti: I believe this is a case of Reiter's disease. In our small country of Finland we have seen in a short time 300–400 cases of this disease, all in connexion with an epidemic of Flexner dysentery, affecting about 250,000 persons. The disease was definitely non-venereal, mainly localized to the joints, eyes and urethra, but also frequently accompanied by various skin lesions. I do not know whether Reiter's disease is a syndrome, which might accompany also other enteric infections, or whether it is a disease *sui generis*. Recently a case of Reiter's disease was seen at Hammersmith Hospital. The patient had no symptoms of dysentery, but the complement-fixation test was weakly positive.

Our cases of Reiter's disease developed during or after the dysentery, in mild as well as severe cases. The clinical course varies in duration and intensity. The joint lesions are nearly always multiple, and may be slight or severe enough to resemble rheumatoid or gonorrhœal arthritis. In our cases the knees and ankles were chiefly affected. Large effusions were often seen, as also noted in to-day's patient. The dermatitis was at times slight and greyish coloured; in other cases severe pustular eruptions occurred. The genital lesions were mostly confined to a slight urethritis

rate in the degenerate nerve, this would be compensated by a constant fractional increment of stimulus intensity at all points of the intensity scale.

This argument, therefore, leads us to expect that the sensitivity loss, or deafness of the affected ear in a case of diffuse degeneration of the VIII nerve, would be constant throughout the intensity range. In fact, the Loudness Recruitment phenomenon would be absent in accordance with our own experimental findings.

It is necessary to add two amendments to this general statement of theory.

It is unlikely to apply at low intensity levels near threshold, where the sensitivity of the ear to small intensity differences is changing rapidly. At high levels, too, it would seem inevitable that a saturation point would be reached very soon in the case of the degenerate nerve, above which no further increase of loudness perception would be obtainable.

This latter point is in good agreement with the finding in some of our cases of a fixed upper limit of loudness in the affected ear.

The highly schematic character of our hypothesis need not be stressed. It would indeed appear evident that loudness grading depends upon a grading not only of fibre numbers but of discharge frequency in the fibres themselves, the resultant being a grading of the total number of nerve impulses reaching the cochlear centres per unit time. While this may be the case, it is doubtful whether it would seriously affect the general validity of our hypothesis.

Thus, while a certain degree of nerve degeneration may lead to a definite fractional decrease in the number of cochlear fibres activated by a sound stimulus of given intensity, it is likely, also, to lead to a definite fractional decrease in the discharge frequency of these surviving fibres, and the combination of these two effects will result in a fixed fractional decrease in the total number of action potentials reaching the cochlear centres per unit time.

This decrease will be compensated and loudness loss restored in the manner of our experimental findings by a fixed fractional increase of stimulus intensity over a wide range of the intensity scale.

SUMMARY

Loudness balance tests were carried out in

(a) 30 cases of unilateral deafness due to Menière's disease.

(b) 20 cases of degeneration of the VIII nerve, due to neurofibroma of the VIII nerve and other varieties of space-occupying lesions of the cerebello-pontine angle.

Results.—Loudness Recruitment was found to be present and complete in all 30 cases of Menière's disease.

Loudness Recruitment was found to be absent in 14 of the 20 cases of VIII nerve degeneration. In the remaining 6 cases it was present but incomplete.

Loudness Recruitment was thus shown to be characteristically present in a disorder of the end-organ of hearing and to be characteristically absent in a disorder of the cochlear nerve fibres.

This latter finding sharply controverts existing views upon the neurological mechanism of recruitment. The practical and theoretical significance of the experimental results is discussed. New hypotheses are advanced in explanation of these results and are based upon recent experimental work on the physiology of hearing and upon the known pathology of the cochlea and VIII nerve.

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The following took part in the subsequent discussion:

Mr. T. Gold; Mr. E. D. D. Davis; Mr. D. W. C. Northfield; Dr. C. Worster-Drought; Dr. C. H. Edwards; Dr. N. G. Hulbert; Dr. G. D. Dawson.

Dr. Overton's case we have decided hypercholesterolaemia, and surely one of the aims of treatment ought to be to diminish the cholesterol in the blood and keep it down fairly to normal. Not only that, but the patient is fat, with a history of diabetes in the family. She surely ought to keep her weight down and keep herself in as good general condition as she possibly can.

The cardiovascular system in these cases should be specially considered; the patients may die of cardiovascular xanthomatosis or atheroma. A man with xanthomatosis very like that of Dr. Overton's patient recently told me that his brother had had the same xanthomatosis as he had, but had got better without any treatment. However, the brother had had to have amputation for ischaemic gangrene (probably due to atheromatous obstruction) of one foot. One of our colleagues had similar cutaneous xanthomata at the elbows and got better for a time, but then suffered from intermittent claudication of the legs, which was found to be due to atheroma (atherosclerosis) at the lower end of the aorta.

The dietetic treatment should be such as, if possible, to avoid hypercholesterolaemia, and there is no reason why, if a patient is being treated in that kind of way, small minimal doses of thyroid should not also be given a trial.

Purpura with Capillary Fragility.—H. W. BARBER, F.R.C.P., and J. D. EVERALL, M.R.C.S., L.R.C.P. (Case-history by Dr. Barber.)

N. J. R., aged 23. Formerly Able Seaman.

30.11.45 : His eruption, which still persists, had been present for three months and had appeared first on the arms. In childhood he had been subject to tonsillitis, and his tonsils had been removed seven years previously. He had been given a course of penicillin injections (one injection daily) after which the eruption cleared almost entirely from the chest and partly from the back. Investigations: Hb 100%; R.B.C. normal; W.B.C. 15,400; Platelets 200,000; Bleeding time 3 mins.; Clotting time 6 mins.

At that time, therefore, there was a considerable leucocytosis, the platelet count was at the lower limit of normality, the bleeding-time was about normal, and the clotting-time was slightly prolonged.

The eruption, which was widespread, involving the trunk and limbs, bore a striking resemblance to Schamberg's disease and to that provoked uniquely by adalin. It was, however, much more purpuric than these eruptions. I suggested that it might be due to a latent haemolytic streptococcal infection, and that a course of penicillin injections in full doses should be given.

In my absence, the patient was seen by Dr. Allan Yorke, 21.6.46. Investigations for a haemolytic streptococcal infection proved negative. A second course of penicillin (30,000 units five times daily for five days) again cleared the eruption on the chest, abdomen and back, but the arms were unaffected. Dr. Yorke noted the resemblance to Schamberg's disease, but compared the case with those seen in the Army in which a purpuric eruption, associated with marked capillary fragility, was apparently provoked by contact with the uniform. Patch-testing with his uniform, pyjamas and blankets, however, proved negative.

I saw him again myself on 3.10.46 and concluded that the eruption resembled Schamberg's disease more than anything else. As regards alternative diagnoses: Hutchinson's "infective angioma" or angioma serpiginosum, of which I showed a beautiful example in a child some years ago, is clearly, I think, a naevoid condition; Majocchi's disease begins on and is usually confined to the legs, and some atrophy is often a sequel to it; Gougerot and Blum's "Pigmented purpuric lichenoid dermatitis" is a diagnosis I have never made, but in our patient there are no lichenoid papules.

The most remarkable feature is the capillary fragility so that purpuric spots may be readily produced on the forearm by compressing the upper arm at a pressure of 100 mm.Hg or by pinching the skin. I have not personally investigated undoubted cases of Schamberg's disease from this point of view.

and penile erythema. In some cases prostatitis, cystitis and hydronephrosis occurred. Conjunctivitis was usually mild, but sometimes severe keratoconjunctivitis and iritis were seen. The duration varied from four weeks to two years. The joint lesions persisted longer until Reiter's disease finally developed into a simple arthritis.

Early in the epidemic the symptoms were often mistaken for gonorrhœa. In a patient with urethritis, eye lesions, joint lesions and skin lesions resembling keratoderma blennorrhagica, one should not feel too sure about gonorrhœa, when the smears are negative and the complement-fixation test is also negative. Most of these patients are young soldiers. If they have conjunctivitis, a joint lesion or dermatitis they are not much concerned, but if they also have urethritis they become "venereal-minded", think about their last exposure and believe they have gonorrhœa. The doctors are often willing to accept this diagnosis. Many of our cases were treated as gonorrhœal and appeared to improve with sulphonamides and penicillin, but they got worse after a while. Our experience is similar to that of Bauer in Los Angeles, who described increased hypersensitivity with peculiar skin lesions resembling those in to-day's case during treatment with sulphonamides. Finally I think the crops of blisters on the soles of both feet in to-day's patient are characteristic of Reiter's disease.

In Finland the disease showed a decided tendency to spontaneous healing in most cases. In severe cases various forms of treatment were tried, generally without any clear-cut effect. We became convinced that the only treatment of any value was fever treatment, such as was used in the treatment of gonococcal arthritis before the discovery of sulphonamides and penicillin. The patient at Hammersmith Hospital had his first attack five years ago and his second attack three years ago. In the second attack, having been ill for fourteen weeks and treated with sulphonamides and penicillin without benefit, fever treatment was applied with the Kettering's hypertherm. Within forty-eight hours there was a dramatic improvement.

Familiarity with Reiter's disease makes one realize that one is not dealing with the first attack; the patient recalls similar attacks before, even as long ago as twenty years. As a rule these attacks were associated with venereal stigmata, in spite of repeated negative smears and fixation tests.

Dr. H. W. Barber: Personally I regard this case as one of arthropathic psoriasis. I think the eruption in the groins is the type of psoriasis that is so apt to be diagnosed as seborrhœic dermatitis.

Xanthoma Tuberosum Multiplex.—JAMES OVERTON, M.D.

Mrs. B. E. G., aged 56. In July 1947 a number of pinkish nodules appeared on the elbows, knees and big toes. She felt "off-colour", with loss of energy and mild dizzy attacks. She also noticed that the skin of her face, antecubital fossæ and flexor aspects of wrists was assuming a dirty brown tinge. For the last few years, and especially in recent months, her weight has been steadily increasing. No loss of hair or dryness of skin. Appetite good; ? increase in thirst. Nocturia $\times 2$; bowels normal.

Family history.—Patient's mother suffered from diabetes mellitus. No knowledge of members with xanthomata.

Personal history.—Menopause three years ago.

On examination.—An obese, lively, jovial woman. Scalp hair and eyebrows normal. Yellow coloration of soft palate. Diffuse, dirty brown pigmentation of face, neck, antecubital fossæ and all aspects wrists. Xanthoma papules and nodules on both elbows, umbilicus, buttocks and patellæ, with linear xanthomata in creases and webs of palms and soles.

B.P. 190/105. General medical, urine and X-ray examination of skeleton and gall-bladder revealed nothing else abnormal.

Fasting blood sugar, blood sugar curve, blood urea, blood sodium and chlorides, and liver function tests were all within normal limits.

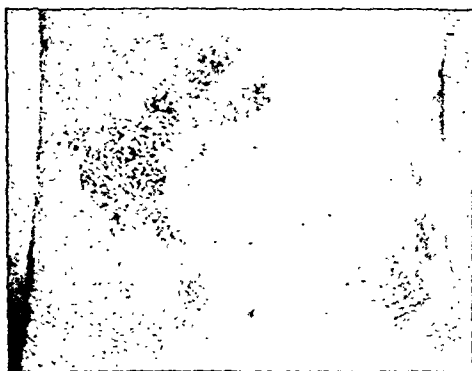
Blood cholesterol on 11.11.47 was 520 mg. % and on 12.3.48 it was 920 mg. %.

W.R. negative.

Dr. F. Parkes Weber: I agree with Dr. Overton that this is an absolutely typical case illustrating the commonest kind of Thannhauser and Magendantz's (1938) hypercholesterolemia group of primary or essential xanthomatoses.

I believe that in hypercholesterolemic cases treatment is of the greatest importance. It may be very disheartening, but, on the other hand, it may do good and very likely prolong life. In

entity. They had previously described their first case in 1925 as "purpura angio-scléreux prurigineux avec éléments lichénoïdes". The essential features of the condition may be briefly summarized. The eruption, which runs a very chronic course but with a tendency to eventual cure, consists primarily of small, slightly raised, smooth, shiny lichenoid papules which are initially pink, but become orange



[Photograph by Dr. W. G. Millar

FIG. 1.—Medial aspect of left lower leg.

and then purpuric and later pigmented. The individual papules do not enlarge and may remain discrete, but often become confluent in irregular plaques. The legs are the commonest site, and the eruption may, as in our patient, remain localized to one leg, but in some cases small discrete papules are widely distributed over arms, legs and trunk. Pruritus is usually absent.

We have found reports of 9 cases in the literature since 1929. In some of these cases the diagnosis seems questionable as venous hypostasis was present. Of the recorded cases, 8 were males and 5 females, and the majority were adults between 30 and 50 years of age, but Senebar and Caro's patient was a girl of 14.

Where the histological appearances have been examined they have been similar to those described above.

The differentiation of this condition from Schamberg's disease is sometimes difficult. Schamberg himself considered that it was an allied condition, but that it was not the same as his pigmentary disease, in which papules are absent.

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Primary Focus of Tuberculous Infection in the Skin.—R. M. B. MACKENNA, M.D.

V. F., female, aged 11, complaining of a swelling in the neck near the left angle of her jaw.

Family history.—An aunt was said to have tuberculosis.

Patient's previous history.—Nothing relevant.

History of present condition.—In December 1947 a small spot appeared on the left cheek just in front of the ear. Four weeks later the swelling appeared in her neck. She was admitted to Oster Hills Hospital under the care of Dr. A. W. Franklin (to whom I am indebted for permission to show the case), and it was clinically

Dr. Allan Yorke: About a year ago I saw two similar cases.

The first was a young man who developed this eruption on the legs after the removal of teeth for apical abscesses. Further extractions were followed by an exacerbation involving the extremities and trunk. Culture from the sockets yielded hæmolytic streptococci. He was treated with penicillin intramuscularly and the condition cleared.

The second patient was a young girl with a clear history of recurrent sore throats and malaise. A culture from the tonsils revealed hæmolytic streptococci. She was successfully treated by tonsillectomy, and then by penicillin (lozenges and intramuscularly). We took further cultures from the excised tonsils and they too yielded hæmolytic streptococci.

Thus in two cases hæmolytic streptococci were demonstrated. I believe that some of these cases may be allied to subacute bacterial endocarditis. Franks doubts whether the flea-bitten kidney found in this condition is due to emboli. He implies that the capillaries become unduly permeable under the influence of an infecting agent, and suggests that it is a capillary toxicosis; possibly the cutaneous capillaries also may become permeable under the influence of an infecting agent.

Dr. F. Parkes Weber: I believe that this is an example of a condition which I was one of the first to describe—*telangiectasia macularis eruptiva perstans*. But the present case is one of the rare examples in males of early middle age. Such a case was described by Sir William Osler under the heading "*Telangiectasis Circumscripta Universalis*" in a man who had epistaxis (see F. Parkes Weber, "*Osler's Telangiectasis Circumscripta Universalis*", *Internat. Clinics*, 1931, series 41, 2, 131).

Pigmented Purpuric Lichenoid Dermatitis of Gougerot and Blum.—E. W. PROSSER THOMAS, M.D., and ARTHUR ROOK, M.R.C.P.

Ronald S., schoolboy, aged 13. The youngest of 5 children all of whom are healthy. Apart from measles, chickenpox and whooping cough he has always been fit.

About six months ago he first noticed a group of "small dry pimples" just above and anterior to the left internal malleolus. There was some irritation in the area at first but there has been none since then. The original papules gradually coalesced to form a plaque. New papules have continued to appear in irregular groups both in the neighbourhood of the original plaque on the anterior aspect of the leg, and in a new area on the medial aspect of the leg. The papules everywhere tend to coalesce into plaques, which by the confluence of papules at their periphery, extend to fuse with other plaques.

On examination.—The skin lesions are in two groups on the anterior and medial aspects of the left leg, just above the level of the malleoli. They consist of slightly raised shiny lichenified plaques of irregular outline. The largest plaque measures $2\frac{1}{2}$ in. at its greatest length and has an average width of 1 in. All plaques show a brownish-red pigmentation and are purpuric on diascopy. Their original papular components can no longer be distinguished. In the neighbourhood of the plaques there are several irregular groups of small brownish-red lichenoid papules and some small pigmented macules (see fig. 1).

No other lesions of the skin or mucous membranes are present.

General medical examination reveals nothing of significance.

Histological report (Dr. Ian Whimster).—**Epidermis:** Slight hyperkeratosis throughout the section and several small patches of parakeratosis which are separated from the granular layer by normal horn. The granular layer is present throughout the section and appears normal. Slight acanthosis with prolongation of rete pegs. **Dermis:** Infiltration by lymphocytes and histiocytes, fairly generalized in the upper third of the dermis but only round vessels, glands and follicles in the lower layers. Many small hæmorrhages and some free pigment in the upper third of the dermis. Prussian blue stain confirms the presence of free blood pigment.

Comment.—Gougerot and Blum in 1929 published an account of 4 cases of a pigmented and purpuric lichenoid dermatitis which they regarded as a clinical

Section of Psychiatry

President—Professor Sir DAVID K. HENDERSON, M.D., F.R.C.P., F.R.S.E.

[April 13, 1948]

Experimental Investigations in the Endocrinology of Schizophrenia

By R. E. HEMPHILL, M.D., and M. REISS, M.D.

It is not our intention to propose—as the title might suggest—that schizophrenia is an endocrine disorder, but from our work and that of others, there is sufficient evidence to encourage search for endocrinological relationships. It is, however, difficult to find case material that is clinically homogeneous. At first we endeavoured to select our cases because of psychiatric similarity, but, as we have found evidence that cases with an apparently identical clinical picture may have dissimilar physiological patterns, we are endeavouring to classify cases according to physiological patterns, and thereby to specify categories of schizophrenia. The paranoid form of schizophrenia has been excluded from this study.

There must be general dissatisfaction in grouping under the clinical label of schizophrenia cases of unknown aetiology, similar in prognosis and perhaps psychopathology, but with little else in common and many points of individual variation. Although it is far from certain that the schizophrenic illnesses of adolescence have the same origin as those of early adult life or following the puerperium, the only accepted treatment for all types is either the production of extreme physiological stress (as in the shock therapies) or creation of a new neural integration (as in leucotomy). Therefore the indications for and results of treatment should be susceptible to expression in physiological and biological terms.

From the enormous literature on the subject, containing so many facts and so few conclusions, it would seem that this hope is not likely ever to be fulfilled. By and large, all workers have reported physiological abnormalities in a proportion of all cases investigated, but there has been no success in correlating these abnormalities with the clinical appearances.

Unless the pathophysiological phenomena are unrelated to the disorder (which is unlikely), this lack of success is either because the polymorphism of the disease group defeats study, or because in the disease group are different entities treated as one illness, the psychiatric diagnosis acting as a mask, or because the physiological behaviour of individuals is subject to unpredictable variation.

In published research in schizophrenia, unlike research in chronic physical disorders, such as rheumatism or cancer, little account seems to have been taken of

obvious that the swelling in the neck was due to tuberculous adenitis. The glands were aspirated on four occasions and brown sterile pus was obtained on each occasion.

Histological report on the skin lesion (Dr. J. W. Whittick).—Within the dermis of both fragments there is a tuberculous reaction consisting mainly of epithelioid cells, occasional multinucleate giant cells and a few peripheral lymphocytes. There is a small amount of necrosis at the centre.

Mantoux test: Six weeks ago 1 : 10,000 negative. One week ago 1 : 10,000 negative.

X-ray (Chest): No evidence of tuberculosis past or present.

Treatment.—Calciferol 50,000 units twice daily has been administered; the cutaneous lesion has retrogressed and the condition of the neck is very satisfactory.

The following cases were also shown:

Lentigo Malignum.—Dr. J. E. M. WIGLEY.

Lymphoblastoma of Cheek.—Dr. JAMES OVERTON.

(1) **Median Mental Sinus**. (2) **Scalp Ringworm Simulating a Patch of Scurf**.—Dr. ALAN LYELL (for Dr. C. H. WHITTLE).

Lipo-melanin Reticulosis of Pautrier Woringer.—Dr. R. M. B. MACKENNA.

Acanthosis Nigricans.—Dr. R. M. B. MACKENNA and Dr. I. ROXBURGH.

Leishmaniasis with a Long Incubation Period.—Dr. LOUIS FORMAN.

Multiple Superficial Basal-cell Carcinomata.—Dr. P. J. FEENY.

(1) **Keratotic Nævus**. (2) **Large Pigmented Nævus of the Scalp**.—Dr. R. E. BOWERS.

Darier's Disease.—Dr. STEPHEN GOLD.

Granuloma Annulare in a Boy of 11 Years Treated with Vitamin E.—Dr. CLARA M. WARREN.

[These cases may be published later in the *British Journal of Dermatology*.]

schizophrenia with constant clinical characteristics, patiently elucidated biochemical correlates. To establish other clinical categories by psychiatric examination alone is probably impossible, but we believe that physiological patterns will emerge from widespread research, by which groups of corresponding cases can be identified without the necessity of relying on the clinical appraisalment.

Published reports show that if various biochemical tests, for example, insulin sensitivity and sugar tolerance, are repeated frequently in schizophrenic patients, there is much day-to-day variation in results, and from clinical experience we know how unpredictable is the response to insulin treatment. If tests are carried out on a large series of patients, significant deviations occur in a greater proportion than in normal controls.

To express these facts in a different way, it is clear that there exist many cases of schizophrenia whose physiological equilibrium is inconstant and a proportion in whom it is constant, irrespective of whether the results of tests are themselves within or without the normal range. It is the factor of inconstancy that operates so strongly against biochemical research. However, we think these schizophrenic patients could be grouped profitably into those with constant and those with inconstant biochemical patterns. Inconstancy might be significant of active, and constancy of arrested disease, or the opposite; or a biochemical pattern might be established at a certain stage of the disease, or it might be characteristic of a certain type. Therefore, much variation in research results is to be expected unless the patient material is in the same stage of the disease or suffering from the same type—conditions clinically unascertainable. If tests could be devised which, repeated frequently, would reveal constancy and inconstancy, it should be possible to spot patients with similar physiological patterns who could then be subjected to extensive and detailed investigations.

The amount of 17-ketosteroids excreted in twenty-four hours bears some relation to the activity of the adrenal cortex and the testis. Its estimation was chosen in preliminary investigations as the master test for the study of constancy and inconstancy as well as to give information about endocrine activity. In previous investigations (Hemphill, Macleod and Reiss, 1942) it had been observed that the output of 17-ketosteroids increased after electro-shock treatment, leucotomy, and occasionally even testis biopsy.

This increase is not, as we thought at first, a regular result of successful electro-shock treatment. We have seen increases even up to three times the normal. This suggested that the daily level of 17-ketosteroid output might vary in schizophrenic patients in whom the biochemical pattern was inconstant.

In a large series of patients of different types many daily analyses of the 17-ketosteroid excretion were made. There was in some of them a day-to-day variation, some showed a rather constant behaviour. It is not yet possible to isolate from these results any particular pattern of variation. Fractionation of the different 17-ketosteroid excreted appears to be more promising at present. The figure gained for the total 17-ketosteroid excretion in twenty-four hours is a resultant only of the different fractions, some of them produced in the testicles, some of them in the adrenal cortex, and some being inactive intermediary products of the steroid metabolism not yet formed to a specific hormone by a ductless gland.

A recently published method of Dingemans and co-workers (1946) was applied for fractionation. In this method a chromatographic separation of over 20 different ketosteroids is possible, including the separation of androsterone and dehydroandrosterone, the former produced mainly by the testicles, the latter by the adrenal cortex. Our fractionation experiments showed that even if different individuals excrete exactly the same amount of total 17-ketosteroids, this total figure might

the duration and stage of the disease; nor do many papers show that the end-result was of consequence to the investigators after the research programme had been carried out, and investigations do not seem to have been conducted on many patients in apparently total remission. There has been much study of phenomena such as circulation, oxygen consumption, and liver function, considered in isolation. Merely to add to the multitude of such investigations could contribute little, and, although we have applied methods of research to isolated phenomena, we have tried to direct our research by biological or endocrine indications.

In recent years we have studied pathological changes in the testis in schizophrenia (Hemphill, 1944; Hemphill, Reiss, Taylor, 1944). Biopsy specimens consistently showed an abnormal histological picture in schizophrenia of early life. The pathological changes were not found in other mental disorders, nor were they marked in paranoid schizophrenia. They were maximum in younger patients and where the prognosis was bad or the disease process far advanced.

The advantage of the biopsy method, in that fresh material can be procured from patients selected at any stage of the disease and in any state of health, is somewhat offset by the small portion of tissue available, for biopsy specimens are too small to enable one to express an opinion about the interstitial elements and Leydig cells. The striking abnormalities were: gross disorder of spermatogenetic elements, with destruction of many tubules, hyalinization of basement membrane, and infertility. The only parallel picture in humans is found in senile testes, but there were points of histological similarity between the schizophrenic testis and that of the animal after partial hypophysectomy. It therefore appeared likely that the testis atrophy was due to abnormal anterior pituitary activity, the normal hormonal control of spermatogenesis and testis development being disturbed.

Attempts to repair this testicular disorder by hormone treatment were not entirely successful. Follicular stimulating hormone (Gestyl) influenced the cells, causing many to increase in size and stimulated spermatogenesis, but complete maturation was not re-established.

The testis structure remained pathological as was to be expected, for the disturbance occurring in adolescence was likely to be complex involving different gonadotrophic, adrenotrophic and other hormones. Simultaneous estimation of anterior pituitary hormone excretion could only be carried out on a selected number of cases; such a programme is in fact nearly impracticable, as the consumption of animals and time appears quite prohibitive. Reference will be made later to some attempts to develop newer and more sensitive methods of assaying anterior pituitary hormones.

A very extensive battery of tests, thorough biochemical investigation of the blood and urine calculated to mirror the physiology of the patients and indirectly to throw some light on anterior pituitary functions combined with the estimation of the excretion of 17-ketosteroids and of cortin-like substances, was employed. No definitely conclusive information was gained by these procedures about pituitary disorder. They did reveal, however, the importance of constancy and inconstancy in physiological patterns and a possible correlation between steroid hormone metabolism and some forms of schizophrenia.

Up to the present the only biochemically-controlled clinical type of schizophrenia yet described is that of Gjessing. He selected cases suffering from the rare periodic catatonic illness and, after repeated physiological investigations, showed that a disturbance of nitrogen balance was associated with psychotic phases. Administration of thyroid to discharge nitrogen retention was accompanied by remission of mental symptoms. Gjessing, therefore, having succeeded in isolating a type of

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significant individual variation, as well as daily or weekly variations in the same patient, in schizophrenics as a whole, and work is being done to show how these changes are related to the fractionated 17-ketosteroid output.

In the case described above, there was a sharp rise in blood cortin after treatment with testosterone. This in its turn might account for the increased muscle activity, although it should be noted that in the other patients the normal level of blood cortin was not associated with the same result.

The catatonic state.—The catatonic state might be the result of a central neurophysiological process or influenced by hormone dysbalance. It might, however, be caused by inhibitory substances in the blood, giving a picture that masks the true illness. Experiments were devised to test the last possibility. Special cages were constructed to contain a rat comfortably. The base of the cages was a large rubber tambour, connected with a kymograph. The slightest movement in any direction agitated the tambour and was recorded on the kymograph. Simultaneous records were made of the activity of six rats, each time under standard conditions of complete quiet. By adjusting the speed of the kymograph, the amounts that the rats moved in twenty-four hours could be assessed from the kymograph record, and therefore the total activity estimated and expressed by % activity. The rats were then injected with blood from catatonic patients, and from normal controls. This experiment is still proceeding, but so far there has been no evidence of inhibitory substance, and in some cases the activity of the rats has been significantly increased by catatonic blood.

Thyroid function in schizophrenia.—Estimation of B.M.R. in schizophrenia is practically valueless, and until recently it has seemed impossible to get a true index of thyroid activity. It is important to do so, for, as we know, a proportion of schizophrenic patients respond to thyroid treatment for a time and in many a tolerance of thyroid develops after treatment for a few weeks. It is not clear whether this anomaly is due to a failure of reactivity or some special property of the schizophrenic thyroid itself. Clinical hyperthyroidism is rare in schizophrenia, and in the few cases we have seen and reported there was eventual recovery. We have felt justified in regarding hyperthyroidism with schizophrenia as a separate clinical entity (Hemphill, 1942).

Reliable methods for the determination of the thyroid function should be the determination of the protein-bound blood iodine, determination of the iodine uptake of the thyroid and determination of the iodine excretion. As a result of more than a year's work a modification of the method used by Taurog and Chaikoff (1946) was finally adopted as the routine method for the investigation of the patients. The iodine uptake and iodine excretion are being investigated with the radio-active tracer technique. A combination of all three methods should give reliable evaluation of the thyroid function. The methods were unfortunately not available at the time when the bulk of the early work on the fractionation of ketosteroids was being done.

Enzyme systems.—In recent years enzyme activity has received much attention. Some workers have speculated that many of the somatic deviations in schizophrenia originate in enzyme abnormality. Richter and Lee (1942), having studied cholesterinase levels in blood, showed that cholesterinase could be an indicator of autonomic activity, as well as of muscular activity. Contrary to the findings of previous workers, notably Stedman and Stedman (1935), we have demonstrated true cholesterinase in C.S.F. (Reiss and Hemphill, 1948).

We have investigated the levels of true and pseudo cholesterinase in blood and in C.S.F. in more than a hundred patients, suffering from different mental disorders,

be arrived at by the excretion of entirely different components. There might be, for instance, a complete lack of dehydro-androsterone excretion, the total sum being made up of an unspecific or not yet completely identified ketosteroid.

The fractionation method of Dingemans was carried out on a great number of patients' urine extracts, but it has not been established as a routine method for research in our laboratories, owing to the unreliability of the various absorption materials obtainable to-day. The method as it is now being carried out consists of separation into ketonic, non-ketonic, alpha and beta fractions; a procedure much better suited to routine work and which gives valuable differentiations.

A group of six chronic catatonic patients, mute and cataleptic for years, who had failed to respond to recognized treatments, were chosen for special examination. They were as nearly similar in state of health, nutrition, and clinical picture as possible, and they were investigated under standard conditions. They were kept under control for several months, during which time fractionated ketosteroids were investigated frequently, and a battery of biochemical tests was applied. Urinary cortin excretion and other hormones were also studied. Although clinically these patients were identical, their fractionated ketosteroid patterns were not so, and in one patient no dehydro-androsterone was excreted.

K. B., aged 33. He had not spoken for eight years, he was practically immobile, and could only just feed himself. Testis biopsy had shown gross atrophy and infertility, with marked sclerosis of small vessels. Total ketosteroids remained within normal limits, but fractionation consistently showed no dehydro-androsterone, the total ketosteroids therefore having little physiological value. The question was, did he produce no dehydro-androsterone, or was it broken down in the body and not excreted? He was treated with 25 mg. daily of testosterone. His ketosteroid pattern altered, and he started to excrete dehydro-androsterone. This more normal pattern is maintained as long as he is under treatment. The change was accompanied by a remarkable clinical improvement. He became active, walked easily, talked and worked. He discussed literature, and asked for chocolates and cigarettes. He put on weight, his circulation improved, and his beard began to grow. He has not recovered, but this partial remission has remained now for about a year. He tends to relapse if not treated with testosterone. His testes are firm; biopsy shows a very abnormal but remarkable picture, unlike anything we have seen before. The testis has been influenced but not repaired.

Administration of testosterone to the other patients in the group, in whom the picture was clinically the same, and who already excreted dehydro-androsterone, failed to produce any clinical response beyond a tendency to auto-erotic behaviour.

It is reasonable to assume that in this single case there is a close relationship between the abnormal endocrine state and the clinical condition. Partial correction of the former produced a maintained improvement in the latter.

Without biochemical control, empirical treatment of these patients with testosterone would have produced the same result, but we would not have been able to suggest why treatment succeeded in one case and not in the others. We see in this an explanation for the occasional successes of haphazard hormone treatment in schizophrenia, observed by Hoskins and most other workers.

One can optimistically speculate that if our methods of analysis were sufficiently accurate we could find definite indications for treatment in many cases. Probably the endocrine disturbance is not simple, and might have to be corrected with the administration of more than one hormone; nor do we know whether a successful result is due to the direct action of the hormone administered, or to its effect in altering the hormone balance.

Cortin in blood and urine.—Heard, Sobel and Venning (1946), and Talbot *et al.* (1945) have described methods for determining cortin in urine by chemical means depending upon the reducing properties of the side chain. Hemphill and Reiss (1947) have made use of the same principles to determine cortin in blood. We have found

constitution is usually good, as evidenced by the fact of marriage, and in the clinical histories there is seldom evidence of a bad or schizoid constitution; the physique is frequently normal; it is the one form of schizophrenia that comes under treatment regularly within a few days or weeks of the appearance of psychotic symptoms; the prognosis should therefore be most favourable. In point of fact, the prognosis is probably worst of all schizophrenic illnesses, and in our survey in Bristol few cases of clear puerperal schizophrenia appear ever to have recovered.

Of 117 cases of puerperal mental illness of various kinds treated at Bristol Mental Hospital in recent years, 21 suffered from schizophrenia; 2 of these made doubtful remissions, and the remainder became chronic and degenerated in spite of insulin and shock treatment. Of the remaining 96 non-schizophrenic reactions, 92 made complete recoveries; 2 died of pneumonia; and 2 improved but were lost sight of after leaving hospital.

Puerperal schizophrenia follows an acute physiological event; we would suggest that this event is not childbirth, but sudden loss of placenta. That the illness responds so badly to insulin and other treatments indicates that the physiological abnormality has some special quality. This special feature might be related to the placental loss. Most animals eat the placenta. Man does not do so, because presumably in the human the acute loss of placental hormone is bridged temporarily from other sources while endocrine equilibrium is being established. It is interesting to speculate that if the schizophrenic constitution represents a more archaic type of functioning, there is a greater demand than normal for the placenta to readjust endocrine balance.

Puerperal schizophrenia logically should be an entity in the disease group and, as there is a minimum of uncontrollable extraneous factors, most suitable for hormone investigation. These patients are so unco-operative and difficult to nurse that collection of urine is not easy and research may be impracticable. However, in some cases we have found evidence of marked deficiencies; in some cases absolutely no oestrone or pregnandiol has been recovered from successive urinary specimens. There are reports of at least two cases in the literature who recovered after immediate treatment with progesterone (Blomberg and Billig, 1942, Schmidt, 1943). There is, therefore, some clinical and biological evidence to support the theory that puerperal schizophrenia is an entity with a particular endocrine basis, in which replacement therapy may be practicable.

It is still worth considering what actually happens in the brain after an endocrine disturbance that could be responsible for the development of mental changes. Attention in this direction is centred around the brain circulation and the brain metabolism. Model experiments carried out in our laboratories on the brains of rats (Reiss and Rees, 1947) have shown disturbance of the economy of the metabolism. Hexokinase activity and glycolytic activity are increased after hypophysectomy. The brain uses more of its carbohydrate reserves, a state which consequently may lead to a breakdown of certain brain functions.

Summary.—In this rather scattered survey, we have endeavoured to show some of the lines along which our research is being planned, and to mention what we have found productive.

We have avoided any mention of the obvious question as to the location of a disease process that operates sometimes through endocrine channels. However, it is not difficult to offer a physiological explanation for some of the psychological phenomena.

A reduced awareness and responsiveness to environment allows the appearance of dream-like states, so similar to schizophrenic thought content. Reduced awareness

including schizophrenia, and during and after experiences such as electro-shock treatment.

In the schizophrenic group, deviations are still being studied. If it is true that cholesterinase levels reflect autonomic activity, we have now another instrument for studying this important aspect of neurophysiology in schizophrenia, and examining the assumptions of autonomic dysbalance in this disorder.

To summarize this section of the work, we feel that with methods for fractionation of 17-ketosteroids and estimating blood and urine cortin, protein-bound blood iodine, cholesterinase in blood, and in C.S.F., and tracer technique with radio-active iodine, we have methods with which to approach the physiological problem in a more definite and refined way than ever possible before.

Investigation of isolated phenomena is not likely to be helpful, and these methods will have to be used in combination. They should be exhaustively applied in the course of and after treatment, and it will be necessary carefully to investigate patients in full remission and at intervals after discharge from hospital.

Relationship of growth and physical constitution to schizophrenia.—In the many studies of physical constitution in schizophrenia allowance does not seem to have been made for the possibility that as the result of the disease process the physical constitution might have changed. Body measurements in psychotic patients, irrespective of the duration of illness or the age, are usually classified together under the respective clinical headings. It is our impression that some patients change shape during the illness and become more leptosomatic.

If the atrophy of the testis is due to faulty anterior pituitary regulation, it may well be that the regulation of growth hormone is upset as well. It is quite plausible that a schizophrenic patient becomes leptosomatic if the disease process begins before growth is complete and not because he is primarily of leptosomatic constitution.

In planned research, cases of schizophrenia should be measured and photographed according to standard scales, with an X-ray control, the procedures to be repeated every six months up to say five years. Analysis of anterior pituitary hormones and growth substances should be made on cases showing an abnormal physical development. This work could be conducted on a large scale in collaboration with other mental hospitals, and it is an item in our research programme in Bristol. The tremendous difficulty in planning a reliable scheme of measurement is evident. Non-psychotic siblings should be included in family controls.

Continuous efforts have been made to improve the methods for the assay of pituitary anterior lobe hormones in the body fluids. One is faced in this work with the difficulty that large volumes of urine or blood are necessary for tracing small amounts of hormone and many animals are required. It was important to find test objects sensitive to small amount of hormones and therefore requiring smaller amounts of body fluids. At present in our laboratories the total hormones are absorbed on permutit. After passing several litres of urine through such a permutit column the concentrated total amount of growth hormone, gonadotrophic hormone and corticotrophic hormone can be gained in a few ml. of the eluate. The method has already been worked out for corticotrophic hormone assay (Cooke, Graetzer and Reiss, 1948).

Puerperal schizophrenia.—Puerperal schizophrenia strikes one immediately as being an important clinical entity, and for various reasons eminently suitable as a research problem. It occurs rarely before delivery and, although commoner in primipara, it is sometimes seen in multipara. It constitutes about one-fifth of all the pregnancy reactions. Its unique characteristics are as follows: the patients are fertile, unlike the majority of comparable males with atrophic testes; the prepsychotic

Section of Experimental Medicine and Therapeutics

President—Professor H. P. HIMSWORTH, M.D.

[February 10, 1948]

Nutritional Œdema

By H. M. SINCLAIR, D.M.

(Wellcome Laboratory of Human Nutrition, University of Oxford)

(1) INTRODUCTION

THE following observations were made in Holland and Germany in the course of work conducted for public health purposes by the Oxford Nutrition Survey. The nature of the work unfortunately precluded the experimental method and the detailed study of a few persons. In the observations in Holland, made mainly in May and June 1945, 3,184 persons were clinically examined of whom 359 (11·3%) had nutritional œdema, 30 (0·9%) had non-nutritional œdema, and 2,795 (87·8%) had no œdema; the German results relate to September 1945 to July 1946 and include an analysis of 10,225 persons of whom 4·1% had nutritional œdema, 4·8% had œdema probably not nutritional, and 91·1% had no œdema. Some results on these persons were communicated to the VII Congress of Biological Chemistry in Liège in October 1946 (Sinclair, 1947).

Three types of nutritional œdema may be distinguished. First, wet beriberi is caused by a diet relatively high in carbohydrate and low in thiamine. Clinically the cases are distinct from the other two types. Secondly, hypoproteinæmic œdema is caused by a low level of protein, particularly albumin, in plasma with a consequent fall in the colloidal osmotic pressure. Low plasma protein, however, does not necessarily cause œdema. The third type may be an early form of the second and is reasonably called famine œdema; the subjects have usually subsisted on diets low in calories and in protein, but they are not necessarily grossly emaciated and the plasma protein values are usually within the normal range. It is this third type that I wish to discuss. But, if famine œdema is defined as pitting œdema that is apparently caused by nutritional deficiency other than deficiency of thiamine and that cannot be ascribed to any non-nutritional cause (such as orthostasis, varicose veins, cardiovascular disease or albuminuria), then the second type as well as the third will be included.

The extensive literature concerning the ætiology of famine œdema cannot be discussed here. The hypotheses include the following: low plasma protein, low colloidal osmotic pressure with normal levels of plasma protein, circulatory failure, increased capillary permeability, renal failure, deficiency of thiamine, pituitary deficiency, thyroid deficiency, and adrenal cortical deficiency.

(2) CLINICAL

History.—The subjects have usually, although not always, lost a considerable amount of weight before œdema appears. They have had nycturia, in which the output of urine is increased. The œdema, which may come on rapidly following cold or exertion, is most commonly noticed as swelling of the ankles in the evening.

Dietary history.—It seems that famine œdema may arise in adults on a dietary intake of between 600 and 1,800 calories a day, with total protein of up to 50 grammes and animal protein of up to 15 grammes. In undernourished persons œdema may be produced, or if present increased, more easily than in normal persons, by administration of sodium chloride—a common observation in Holland and Germany.

Clinical examination.—Famine œdema is very rarely seen in children. Its

is common in fatigue, and in conditions such as the male climacteric, where poor adrenal cortex function or inadequate male sex hormone is causative.

The conception that schizophrenia represents a failure of responsiveness to the environment cannot easily be proved, but test situations such as response to heat and cold can be created. Where there is faulty adaptation, with poor thermal regulation, there should be, on the basis of animal experience, a poor response in the output of cortin, cortin levels being used as an index of physiological adaptability.

Some such experimental planning might serve the dual purpose of extracting from the great mass of schizophrenics those with poor responsiveness and those with good, and thereby act as a guide to prognosis.

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Clinical examination.—Famine œdema is very rarely seen in children. Its

incidence increases with age; and it is of course much commoner in males than in females if their dietary intake is equal in amount. Table I shows the incidence of œdema as found in the examination of random samples of the population in particular areas of Leiden and The Hague.

TABLE I.—AGE AND SEX INCIDENCE OF FAMINE (ŒDEMA) (%) (HOLLAND)

Degree of œdema		Age-group	Males			Females		
			20–	45–	60–	20–	45–	60–
Leiden	Mild	..	3	11	32	7	21	31
	Marked	..	0	3	10	0	1	7
Hague	Mild	..	5	18	49	5	23	41
	Marked	..	0.6	3	7	0.3	1	5

Number examined:

		Total all ages						
Leiden	..	1,050	147	69	41	190	89	42
Hague	..	1,488	171	95	84	308	154	120

The common clinical manifestations of undernourishment are usually present, and acrocyanosis of the hands is particularly prominent. We have found no correlation between incidence of famine œdema and the following: thickness of skin and subcutaneous tissue, systolic or diastolic blood-pressure, pulse rate (measured on persons in the same population with no œdema or with non-nutritional œdema).

(3) BIOCHEMICAL OBSERVATIONS

To our surprise we found in Holland that there was no significant difference between the mean values for serum protein and for albumin of subjects with nutritional œdema and those for subjects without; and the mean values fell within the statistically normal range (Table II). The same result was subsequently obtained in Germany.

TABLE II.—MEAN VALUES FOR SERUM PROTEIN AND SERUM ALBUMIN (IN G./100 ML.) OF ADULTS WITH AND WITHOUT (ŒDEMA) (NUMBER OF PERSONS IN BRACKETS)

				Males			Females		
				Famine œdema	Other œdema	No œdema	Famine œdema	Other œdema	No œdema
Germany	Total protein	(densitometric)	..	7.6	7.6	7.8	7.8	7.8	7.8
			..	(76)	(61)	(1,584)	(67)	(201)	(1,385)
	Total protein	(biuret)	..	7.5	7.8	7.7	7.9	7.9	7.8
			..	(26)	(37)	(653)	(29)	(139)	(781)
Holland	Albumin	(densitometric)	..	5.0	5.1	5.0	5.1	5.1	5.1
			..	(25)	(41)	(694)	(31)	(140)	(780)
	Total protein	(biuret)	..	7.24	7.32	7.63	7.63	7.79	7.72
			..	(99)	(5)	(267)	(92)	(9)	(311)
Holland	Total protein	(biuret)	..	7.25	7.3	7.25	7.65	7.85	7.66
			..	(10)	(1)	(15)	(10)	(2)	(7)
	Albumin	(biuret)	..	4.44	4.4	4.62	4.73	4.3	4.81
			..	(10)	(1)	(184)	(9)	(1)	(206)

We intended in Holland to rely for total protein upon the rapid densitometric method of Jacobsen and Linderstrøm-Lang (1940) which we had used for nearly four years and had investigated carefully (*see* Lloyd *et al.*, 1945). Because our values in Holland were unexpected we checked them by estimating protein by four methods: densitometric, gravimetric, micro-Kjeldahl and biuret (*see* Sinclair, 1947); the agreement was excellent. But the density-protein relation for serum or plasma calculated from the first two methods was different from that given by others: Protein = 355 (G - 1.0069) where G is the density expressed in terms of d_{20}^{20} . The comparison between the gravimetric and micro-Kjeldahl methods for blood samples from persons with or without famine œdema showed that the serum protein from the former contained significantly less nitrogen: protein from 11 non-œdematous persons gave an average conversion factor (\pm s.e.) of 6.252 ± 0.067 , whereas for 17 œdematous persons the factor was 6.435 ± 0.046 if two outlying values were omitted and

6.582+0.122 if these were included; in either case the difference is significant. A qualitative change in the serum protein of persons with nutritional œdema has also been proved by Florkin and Duchâteau (1944).

We found in cases of famine œdema that there was a correlation between colloidal osmotic pressure of serum and total serum protein ($r = 0.78$), and we confirmed the observation of Govaerts and Grégoire (1941) that the pressures were lower than those calculated from Govaerts's equation relating them to concentration of albumin and globulin. We found the protein content of œdema fluid was about 0.8 g./100 ml., but it was probably raised because our cases in Holland were not of recent origin. Since Luckner (1938) showed that œdema could be produced in rats on a diet low in protein and prevented or cured by cystine, we estimated this amino-acid in the serum of 64 persons without œdema and 27 persons with famine œdema, but found no significant difference in the levels.

Estimation of various inorganic ions, hæmoglobin, hæmatocrit, certain vitamins, &c., showed no marked differences between mean values for persons with and without famine œdema (Sinclair, 1947), and there was no evidence from the values that hæmoconcentration was causing high values for serum protein in persons with famine œdema.

Simonart (1947) and Heilmeyer (1946) have attributed famine œdema to deficiency of thiamine. In the cases we studied this was not a factor for five reasons: the ratio of thiamine to non-fat calories in the diet was not low; the clinical picture was different; there was no difference in blood pyruvate levels between persons with and without famine œdema; urinary excretion of thiamine gave no evidence of deficiency; therapeutic tests were negative.

(4) NYCTURIA

Persons with famine œdema tend rapidly to lose their œdema through urinary excretion when they are recumbent, and undernourished persons even without pitting œdema complain of nycturia and excrete unusually large amounts of urine at night. Normal individuals concentrate urine more when upright than when recumbent (Erlanger and Hooker, 1904); and this effect of posture is intensified in undernourishment. Govaerts (1947) has shown that persons with famine œdema when erect give a diminished response to Volhard's water test, and there is also a diminished renal excretion of orally administered salt. It was found in Germany that when recumbent they give an increased response to the water test, and Dr. Cunningham will show in the discussion that in these persons the urinary excretion of water and of solids is increased significantly. According to Brun *et al.* (1945), the diminished water diuresis in the passive erect posture is brought about by increased reabsorption of water in the renal tubules through increased secretion of the antidiuretic hormone of the posterior lobe of the pituitary. If this is so, the effect on the pituitary of the upright posture might be intensified in undernourishment. Trueta *et al.* (1947) have suggested that posture or the antidiuretic hormone causes increased tubular reabsorption of water through arteriolar constriction shunting the renal blood-flow from the cortical glomeruli to the juxtamedullary glomeruli which are part of nephrons with long thin loops of Henle and vasa recta that are well adapted for reabsorption of water. In undernourished persons this arteriolar constriction in the upright posture may be intensified. It should be noted that arteriolar constriction is responsible for the acrocyanosis of the hands.

(5) ADRENALS

The changes in the adrenals that occur in undernourishment and in deficiency of thiamine do not seem to have been studied much in recent years. The extensive early literature indicates that in children inanition produces a considerable diminution in size of the adrenals (Jackson, 1922). In adults, simple fasting (in which famine

œdema is not usually found) is accompanied by loss of weight of the adrenals, but deficiency of protein or of salts or of thiamine causes enlargement. With one exception (Enright, 1920), a number of authors have reported enlargement of the adrenals in famine œdema, and the same has been reported for human beriberi; the cortex is mainly affected. McCarrison (1919), as a result of his work on pigeons, concluded "that disorder of the adrenal glands and malnutrition of the tissues are the main factors concerned in the production of œdema in both inanition and beriberi". He likened the adrenal enlargement to that found in the thyroid in iodine deficiency but thought there was an increased production of adrenaline. In pigeons fed autoclaved rice he found the adrenals weighed about 23 mg. in controls, 36 mg. in birds with "dry beriberi", and 68 mg. in those with "wet beriberi". This association with nutritional œdema is striking, and should be further investigated especially as oral administration of salt enormously increases water retention in famine œdema in man and in pigeons deficient in thiamine.

(6) SUMMARY

The rapid examination for public health purposes of a large number of persons during the famine in Holland and subsequently in Germany has shown that in famine œdema the levels of serum protein, of serum albumin and of serum cystine are within the statistically normal range. Protein was estimated by four different methods. Although the colloidal osmotic pressure of serum is slightly lowered, this cannot account for the œdema; the lowering may be caused by a qualitative change in serum protein, the mean nitrogen content of which is significantly decreased in cases of famine œdema.

In two of the types of nutritional œdema, namely famine œdema and wet beriberi, there is enlargement of the adrenals. The nycturia of undernourishment appears to be caused by an intensification of the effect of posture on the kidneys of normal persons: there is increased reabsorption of water in the renal tubules in the passive erect posture. In famine œdema this reabsorption appears to be greater, and when recumbent there is a large excretion of urine. The postural effect might be brought about by a greater secretion than normal of antidiuretic hormone of the posterior lobe of the pituitary or by the renal shunt of Trueta (through the juxtamedullary glomeruli). Further work is needed to settle this.

[The work described here was done by members of the Oxford Nutrition Survey: in Holland, mainly of Mr. B. B. Lloyd, Dr. van der Kamer, Dr. Emmerie and Dr. Engel; in Germany, mainly of Mr. B. B. Lloyd, Dr. D. J. C. Cunningham, Dr. J. C. Thompson and Dr. Widmann. Full particulars will be published in due course by those who did the work.]

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Nutritional Anæmia

By MARTIN HYNES, M.D.

NUTRITIONAL anæmia may be defined as an anæmia due to deficiency of the elementary materials of red-cell formation or of the accessory vitamin-like factors necessary for hæmatopoiesis. It is difficult, however, to translate this definition into quantitative terms, for deficiency depends upon the individual's demands as well as upon the available supplies. A diet which is hæmatologically adequate for a healthy man is often insufficient for a pregnant woman or a victim of hookworm infestation or malaria. Moreover, infections of all kinds are more common when the diet is ill-balanced or insufficient, and even quite trivial infections rapidly cause anæmia, which may therefore be common in the undernourished even when no strictly hæmatological deficiency is present.

Only two of the raw materials of red-cell formation seem to be essential—iron, and protein from which the pyrrol ring and globin fraction of the hæmoglobin molecule can be synthesized. Little is known of the nature of the accessory hæmatopoietic principles, but two classes are clearly recognized—Castle's extrinsic factor, and Wills's factor which is concerned in nutritional macrocytic anæmia. Other members of the vitamin-B complex are necessary for erythropoiesis in some animals, and lack of vitamin C causes anæmia in man.

It is possible to find cases of anæmia due to each of these deficiencies, but a combination of deficiencies is much more common than a single one, and it is often impossible, as well as undesirable, to cure the patient's anæmia without correcting his whole diet.

Iron deficiency.—Iron-deficiency anæmia arises when the loss of iron from the body exceeds the intake. In the individual case abnormal loss is usually a more important factor than deficient intake, but the incidence of iron-deficiency anæmia in a community depends in large measure upon the iron available in the diet, and is in that sense a problem of nutrition. In this country before the war, for example, this form of anæmia was much commoner in women of the poorer social classes, for the cheapest foods—fish and chips and white bread—had a low iron content (Davidson *et al.*, 1944).

The total iron content of a diet is not, however, a reliable estimate of the amount which is physiologically available for hæmatopoiesis. Only ionic iron can be absorbed, so that if a high proportion of the iron of a foodstuff is supplied by organic, porphyrin compounds, only the small fraction broken down into ionic iron by digestion or, more probably, by bacterial action, can be absorbed. The direct estimation of "available" or ionic iron by the α -dipyridyl reaction does not, however, give a reliable indication of the value of a diet as an iron source. A more important factor is the dietary content of substances such as phosphates, certain protein derivatives, and phytic acid, which form insoluble compounds with iron in the intestine.

It is possible to lay down general rules, such as that a diet containing a total of 15 to 20 mg. of iron is adequate for women in this country, but it is important to remember that the nature of the diet is implicit in this statement. The ratio of physiologically available iron to total iron is reasonably constant in a given community, but if the nature and proportion of the foodstuffs eaten are very different the amount of iron potentially available for hæmatopoiesis may be lower even though the total iron content is higher. Hynes *et al.* (1945), for example, found that 64% of 1,400 North-West Indian soldiers suffered from hypochromic anæmia which could be corrected by iron therapy. The total iron content of their diet was about 65 mg. daily, but the composition of the diet was very different from that of Europeans; foods made from *ata* (coarse wheat flour) predominated, and only 1 oz. of meat was eaten daily.

The importance of increased iron loss as a cause of iron-deficiency anaemia is well exemplified in this country by the fact that hypochromic anaemia is rare in men, but is common in women, who suffer the iron losses of menstruation and child-bearing. In the tropics hookworm infestation is a nearly universal cause of blood loss but the infestation, unless exceptionally heavy, only produces anaemia when malnutrition is present. The anaemia can be cured, without worming, by large doses of iron, but it also recovers spontaneously when the patient is given an adequate, balanced diet (Hynes *et al.*, 1946). It seems probable that factors other than a simple increase in dietary iron are involved in this recovery.

A relatively slight decrease in iron absorption may also precipitate deficiency, and we are very familiar in this country with the association between gastric achlorhydria and hypochromic anaemia.

Protein deficiency.—Anaemia can be produced experimentally by protein deficiency, but the anaemia does not arise until the protein reserves are completely depleted and even the plasma protein level is substantially reduced. Such anaemia is due in part to the general lack of protein, and in part to deficiency of lysine, phenylalanine, and, especially, of methionine, which play some essential but ill-understood part in erythropoiesis (Glynn *et al.*, 1945). In practice, however, it is probable that the infections associated with severe malnutrition are a more potent cause of anaemia than protein deficiency itself. Vaughan (1948) has suggested that the anaemia of infection is itself a result of a general disturbance of protein metabolism affecting the synthesis of the globin element of haemoglobin.

Protein deficiency is probably more important as an obstacle to the cure of anaemia than as a cause of it. A patient during recovery from severe anaemia may build some 400 grammes of globin into haemoglobin, an amount of protein equivalent to 4 lb. of steak.

The lack of haematopoietic factors associated with meat may cause the nutritional macrocytic anaemia described below, but meat has other, less defined, roles in blood formation. The addition of extra meat to the diet of Indian recruits, for example, hastened the spontaneous cure of their anaemia, whereas an equal addition of protein as milk was without effect (Hynes *et al.*, 1946).

Nutritional macrocytic anaemia.—A severe and often fatal macrocytic anaemia is common amongst people who live on a restricted and largely carbohydrate diet. It differs in many important clinical and haematological respects from pernicious anaemia, but especially, as Lucy Wills showed, in the fact that it can be cured by large doses of marmite by mouth.

The nature of the haematopoietic principle—Wills's factor—which cures nutritional macrocytic anaemia is still unknown. It is certainly not any known member of the vitamin-B complex, and it is not, as was once thought, identical with Castle's extrinsic factor.

The blood and marrow pictures of nutritional macrocytic anaemia differ clearly from those of pernicious anaemia, and the response of nutritional macrocytic anaemia to highly purified liver extracts such as anahæmin is uncertain and demands at least five times the dose which will cure pernicious anaemia.

In the tropics nutritional macrocytic anaemia is nearly always associated with malnutrition, although it is usually possible to name pregnancy, malaria, or dysentery as the precipitating cause. The fundamental lack seems to be that of some factor associated with animal protein, for in the Indian Army during the last war the disease was much commoner in vegetarians than in meat eaters. When the incidence was highest, as in the earlier Burma campaigns, the lack of fresh meat and milk and the religious prejudice of the Indian against tinned meat had forced most Indian soldiers to live on a purely vegetable diet. The disease was practically unknown.

amongst Europeans in the same army, who willingly ate tinned "bully" and bacon. There is some evidence that milk will prevent nutritional macrocytic anæmia even when no meat is eaten.

Deficiency of Wills's factor alone, however, will rarely, if ever, give rise to nutritional macrocytic anæmia unless the demand for the factor is increased. Napier (1939) has suggested that in chronic malaria the need for blood formation is increased by phagocytosis of red cells by the hypertrophic reticulo-endothelial system. The utilization of Wills's factor consequently increases, and if the amount in the diet is insufficient to meet the higher demand, malformed red cells are produced and still more readily phagocytosed, so that a vicious circle is set up.

Pregnancy may similarly cause nutritional macrocytic anæmia because the mother's diet has to meet the additional demands of the fœtus for Wills's factor. It was the importance of anæmia as a cause of puerperal mortality in India which first drew the attention of hæmatologists to nutritional, or as it was then called, tropical macrocytic anæmia. The rather rare macrocytic anæmia of pregnancy seen in this country may be of the same fundamental nature.

Nutritional macrocytic anæmia may be precipitated by dysentery, which presumably diminishes absorption of Wills's factor. It is not yet clear whether the macrocytic anæmia of sprue is due to deficiency of Wills's or of Castle's factor, and so far as I am aware no study of the bone-marrow has been made by anyone who has grasped the distinction between the megaloblasts of nutritional macrocytic anæmia and of pernicious anæmia.

The treatment of nutritional macrocytic anæmia during the last war was still very unsatisfactory. Moderately severe cases, with a hæmoglobin of 5 grammes per 100 ml. or higher, would often recover spontaneously without any specific hæmatinic treatment when they were given the generous hospital diet and concomitant disease was cured. When, however, the hæmoglobin was 3 grammes per 100 ml. or less the marrow function was not restored by any amount of liver injections, and only repeated transfusions would keep the patient alive. Later reports have suggested that proteolysed liver is as effective in this tropical macrocytic anæmia as it is in the allied macrocytic anæmia of pregnancy seen in this country, and still more recently folic acid has been claimed to be effective. The response of the less severe cases to dietary treatment alone, however, makes the assessment of any new therapy difficult.

Dimorphic anæmia.—Nutritional deficiencies rarely occur singly, and it is not surprising that iron deficiency is often added to nutritional macrocytic anæmia. Trowell has used the name "dimorphic anæmia" for the combined deficiency, to emphasize that the peripheral blood picture combines the features of a megaloblastic and an iron-deficiency anæmia. In practice it is important to recognize that macrocytic anæmia will often not respond adequately to therapy until iron as well as liver is given and that severe iron deficiency may completely mask Wills's factor deficiency unless sternal puncture is used as an aid to diagnosis.

Vitamin deficiency.—Of the vitamins only C is essential to hæmatopoiesis, and the anæmia of scurvy will not respond to hæmatinics until ascorbic acid is given. The infections associated with deficiencies of other vitamins are, however, a very potent cause of anæmia.

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Dr. R. B. Hawes: Dr. Sinclair has definitely demonstrated that famine œdema has no relation to beriberi with which it had so often been confused. It would be a great contribution to progress if the term beriberi were defined so that every ailment that recovered after receiving B₁ should not be labelled as such. True beriberi is a very definite syndrome and should not be used to connote any dietetic deficiency with œdema and neuritis. My experience agrees with that of Dr. Sinclair in that œdema in starving people is often related to the salt intake.

Regarding macrocytic anæmia, when I was treating many cases long before folic acid was discovered, it appeared to me that the condition was related to a deficiency of phospholipoids in the diet and by using one to two dozen egg yolks at a dose I obtained a very rapid regeneration of the blood commencing within forty-eight hours.

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For the night of June 12-13, 1946, every sample of urine passed by the occupants of one barrack room was collected and its volume and specific gravity recorded. The following day blood samples were taken for the estimation of plasma protein and hæmoglobin by the densitometric method of Linderström-Lang; blood-pressures were recorded, and the subjects examined for œdema. Altogether 89 subjects contributed of whom 13 had clinical œdema.

At the time of the investigation the subjects had been for nine months to a year on a diet supplying daily between 1,500 and 2,000 calories and containing 35 to 45 grammes of protein, 4 to 10 grammes of which were of animal origin.

For statistical analysis of the results, the subjects have been divided into three groups: those with clinical œdema (13), those with no œdema but with polyuria (66), and those with neither (10). Polyuria has been arbitrarily taken as 600 ml. or more passed during the night. It is thought that the psychological effect on the "normals" of seeing their companions on the move all night (the total number of micturations in the barrack-room was about 360!) would make them micturate more frequently than they would otherwise have done. The results are as follows:

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From this it is suggested that the majority of the individuals had a disorder of water metabolism in which water and solids were presumably retained during the day and were eliminated during the night. This retention was sometimes sufficient to produce clinical œdema.

Dr. S. E. Dicker: On the assumption that the cell membranes are impermeable to chloride, it is possible to calculate the extracellular fluid phase of muscles. Series of rats were fed for seven, fourteen and forty-two days on a protein-deficient vegetable diet and compared with controls fed on a standard diet. After seven days on the protein-deficient vegetable diet no significant changes could be found in the plasma nitrogen content, the albumin/globulin ratio, the colloid osmotic pressure of the plasma and the total water content of plasma and muscle, but there was a significant increase in the extracellular fluid phase of the muscle, indicating that tissue œdema was present already. After fourteen days on the protein-deficient diet, there was a fall in the plasma nitrogen and in the albumin/globulin ratio, accompanied by a fall in the colloid osmotic pressure, and a further increase in the extracellular fluid phase. It can thus be concluded that the onset of œdema formation in malnutrition is independent of changes either in the albumin/globulin ratio or in the colloid osmotic pressure of plasma. At a later stage further increases of the extracellular fluid phase were concurrent with a progressive fall in the colloid osmotic pressure of the plasma. However, even after forty-two days on the protein-deficient diet, when the plasma protein concentration had fallen by nearly 30% as compared with controls, no clear correlation could be found between the

degree of hypoproteinæmia, the fall of the colloid osmotic pressure of the plasma and the magnitude of the extracellular fluid phase of tissues.

The President: The data presented at this Meeting were in accord with the growing opinion that famine œdema could not be explained entirely on the basis of the classical hypothesis of Starling, that the quantity of fluid accumulating in the tissues depended on the interplay between the colloidal osmotic pressure of the plasma and the blood-pressure within the capillaries, the level of interplay being influenced by the degree of capillary permeability. Some additional factor was indicated and the identity of this was suggested by the observation that ingestion of salt conspicuously increased the degree of famine œdema. This might arise in one of two ways. The transient retention of water normally induced by taking salt tends also to dilute the plasma proteins and, if through under-nutrition these cannot be rapidly restored to normal levels, the consequent lowering of plasma osmotic pressure would allow fluid to accumulate in the tissues. Such an hypothesis could easily be put to test. Alternatively there might be an impaired ability to excrete salt and/or water in undernourished people. Ralli, Robson, Clarke and Hoagland (1945) have demonstrated this in cases of hepatic cirrhosis and further that this impairment was accompanied by an increased excretion of an antidiuretic factor in the urine. This was attributed to failure of the damaged liver to destroy a pitressin-like factor. Following this clue Leslie and Ralli (1947) have shown that rats given a low-protein high-fat diet for two or three weeks began to excrete in the urine increasing quantities of the antidiuretic factor. This occurred long before such diets had produced hepatic cirrhosis and was ascribed to impairment of liver function by fatty infiltration. In view of the results reported by Dr. Dicker of the effects of low-protein diets the impairment might well be due to protein deficiency, and applicable to human cases of starvation.

With regard to nutritional macrocytic anæmia Dr. Hynes had mentioned that a similar anæmia could be produced experimentally by lack of an essential amino-acid such as methionine. The clinical clues indicated a correlation between protein deficiency and nutritional macrocytic anæmia in man. Gajdos (1946) had reported a similar anæmia during the famines in Europe and had observed that it responded to methionine.

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Lieut.-Colonel J. A. Manifold, R.A.M.C.: During the war I was for some time connected with the administrative side of Dr. Martin Hynes' survey work in India. My colleagues and I, while there, were able to make some investigations into severe cases of anæmia affecting Indian troops in a hospital of 7,500 beds. We not only did the hæmatological work but through the kindness of the Officer Commanding the hospital we were also able to control the treatment.

These men were selected base troops not having been exposed to the hæmatological risks of the campaign in Assam and Burma and were on a diet of some 4,000 calories containing 109 grammes of protein (animal 24 grammes). The mean Hb level on reporting sick was 7.22 grammes per 100 ml. and the peak incidence in the second and third year of service. Non-meat eaters were very significantly more susceptible than were meat eaters. At a low Hb level there was a strong association between hookworm infestation, microcytosis and hypochromia and chronic malaria with macrocytosis. Dr. Hynes has indicated the mechanism by which the latter may take place. The former is really a simple iron-deficiency microcytic hypochromic anæmia of the "pile"-bleeding, iron-deficient type. This association did not hold good at high Hb levels.

The suggested ætiology may be expressed in the form of an equation, in which "Precipitating Factors" added to a hypothetical "Unknown Factor" acting in a substrate (probably a poor intake of protein of high biological value and/or a high phytic acid content of the diet) give rise to anæmia. The precipitating factors are chronic malaria and/or hookworm infestation and/or dysentery and diarrhoea and/or pregnancy. These factors are, of course, very common in the agricultural classes in India, and are far more common than are severe cases of anæmia.

The substrate is more or less universal in the tropics and therefore it becomes necessary to postulate an unknown factor which is really a peculiar susceptibility to hæmatological stress, possibly conditioned by protein starvation. Within broad limits the extent of the precipitating factors do not affect the issue.

Various graphs and charts were shown illustrating hæmatological details from cases of this type and attention was drawn to the fact that, within about three months, 62 persons out of 66 suffering from severe anæmia attained an almost completely normal blood picture without any supplementary aids such as blood transfusion. Orthodox hæmatological treatment achieved this end, disproving

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COMBINED MEETING WITH THE

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DISCUSSION: THE EPIDEMIOLOGY OF TRYPANOSOMIASIS IN MAN AND ANIMALS

Dr. J. Carmichael: The trypanosomes which cause disease in mammals can be divided into two large groups, those which are normally transmitted by species of *Glossina* or tsetse fly, and those which are not so transmitted. The epidemiology of trypanosomiasis varies, of course, with each group. From the human point of view Chagas' disease caused by *T. cruzi* and transmitted by the Reduviid bugs is the most important. In South America also there are two important diseases of animals caused by trypanosomes—mal de caderas, a trypanosomiasis of horses caused by *T. equinum*, and a disease of cattle caused by a parasite similar in morphology to *T. vivax* and often referred to as *T. venezuelense*.

The epidemiology of these diseases is obviously closely related to the seasonal distribution of the Tabanidæ. Another important disease of animals is that caused by *T. evansi*, and often referred to as surra. Here again the disease is transmitted by flies belonging to the family Tabanidæ and certain species of *Tabanus*.

The tsetse fly is confined almost entirely to Africa. The most important *Glossinæ* which are responsible for the disease in man and animals are the riverine species *G. palpalis* and *G. tachinoides*. In the open savanna and bush country *G. morsitans* and the closely related species *G. swynnertoni* are responsible for the vast amount of human and animal trypanosomiasis. Recently, however, *G. pallidipes* has become more important and has been incriminated with the animal and the human disease. Other species of *Glossina* such as *G. brevipalpis* and *G. longipennis* are not so widespread but they are important where they exist. In Zanzibar up till quite recently tsetse fly were said to be absent, although many outbreaks of *T. congolense* in cattle kept occurring. Diligent search, however, revealed that *G. austeni* existed in appreciable numbers and was no doubt responsible for the losses from trypanosomiasis. There is no doubt that the starting point of trypanosomiasis both in man and animals is the tsetse fly. Generally speaking, contact with the fly is incompatible with the existence of domestic animals, with the possible exception of the dwarf cattle of West Africa. These animals possess a tolerance to trypanosomiasis but only when they are well cared for. There are, however, large numbers of human beings living in contact with tsetse fly, both the riverine species and the savanna bush types of *Glossina*.

Since the classical epidemic in the Lake Victoria region of Uganda about 1900, thousands of people were moved away from their homes out of contact with the fly, *G. palpalis*, and they were not allowed to return for some twelve to fifteen years, during which time the fly had no human beings to feed on, but confined itself to the fauna which existed on the Sesse Islands and the lake shore. The swamp antelope or sitatunga, in the absence of its human enemies, left the swamps and assumed the habits of its near relative, the bush buck, and provided the fly with food. *G. palpalis* also had crocodiles, varanus lizards, birds, monkeys and small mammals to feed on. It is now well over twenty years since the population returned to quite a number of the islands, and no epidemic has occurred, and it has been suggested that during the intervening period in the absence of man *T. gambiense* has lost its pathogenicity for the human being. It seems to me that even in the presence of the parasite, whether it be *T. gambiense* or *T. rhodesiense*, there must occur in many parts of Africa a balance between host and parasite, and until some adverse

the oft-repeated statement that these types of anæmia do not respond to established physiological principles of treatment, i.e. crude liver extract of the "Campolon type" to the macrocytic cases, and ferrous iron to those iron-deficient and microcytic, aided by a diet rich in protein of a high biological value given to all cases.

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Dr. Nicholas H. Martin: With reference to Dr. Sinclair's paper, it appears to me that what is important in considering the circulation of proteins in starvation is not so much the *percentage* of circulating protein or the *percentage* of circulating albumin and globulin as the absolute amounts of the circulating protein. The need for such an estimate was brought home to me strikingly in the study of protein metabolism in infective hepatitis and serum-transmitted hepatitis (Martin, 1948). I wonder if Dr. Sinclair has any available data of absolute figures of the circulating proteins in his patients?

While it is true that with the more modern and refined techniques no gross quantitative disturbances of protein pattern have been demonstrated in extreme starvation, nevertheless, as Bourdillon predicted and Luetscher demonstrated, there are qualitative differences in the individual "protein" in other diseases. It might be informative to examine the individual proteins in nutritional oedema by the same techniques in the hope of disclosing similar or parallel qualitative differences.

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Major A. R. T. Lundie: I was very interested, in view of personal experience, in the remarks of Dr. Sinclair and other speakers on the ill-effects of the administration of sodium chloride to cases of nutritional oedema.

I should like to know if any explanation can be given for the craving for salt which I have noticed in such cases; and which sometimes proved too strong even for those who suspected that the taking of large quantities of sodium chloride would be unwise.

Dr. Sinclair (in reply): I agree with Dr. Martin about the desirability of estimating plasma volume so that the absolute amount of protein could be calculated. In Holland this was not practical, and from a large number of different determinations of various substances in blood and plasma we concluded that the volume was not greatly altered. In view of the qualitative change in protein that we found in Holland, we tried in Germany to obtain data on the electrophoretic constitution of the protein but with great difficulty. A few samples of serum from cases of famine oedema in Germany were flown to Oxford and examined in the ultra-centrifuge by Dr. Ogston without any abnormality being discovered.

Professor Himsworth's suggestion that there may be a failure of destruction of antidiuretic hormone is very interesting, but I think it is unlikely as there is usually no evidence of liver damage and it is unlikely that such damage occurred within seven days in Dr. Dicker's rats. But an increase in the amount of antidiuretic hormone in the circulation is the most probable hypothesis to explain the increased reabsorption of water and salt in the renal tubules.

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Dr. Nicholas H. Martin: With reference to Dr. Sinclair's paper, it appears to me that what is important in considering the circulation of proteins in starvation is not so much the *percentage* of circulating protein or the *percentage* of circulating albumin and globulin as the absolute amounts of the circulating protein. The need for such an estimate was brought home to me strikingly in the study of protein metabolism in infective hepatitis and serum-transmitted hepatitis (Martin, 1948). I wonder if Dr. Sinclair has any available data of absolute figures of the circulating proteins in his patients?

While it is true that with the more modern and refined techniques no gross quantitative disturbances of protein pattern have been demonstrated in extreme starvation, nevertheless, as Bourdillon predicted and Luetscher demonstrated, there are qualitative differences in the individual "protein" in other diseases. It might be informative to examine the individual proteins in nutritional oedema by the same techniques in the hope of disclosing similar or parallel qualitative differences.

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Major A. R. T. Lundie: I was very interested, in view of personal experience, in the remarks of Dr. Sinclair and other speakers on the ill-effects of the administration of sodium chloride to cases of nutritional oedema.

I should like to know if any explanation can be given for the craving for salt which I have noticed in such cases; and which sometimes proved too strong even for those who suspected that the taking of large quantities of sodium chloride would be unwise.

Dr. Sinclair (in reply): I agree with Dr. Martin about the desirability of estimating plasma volume so that the absolute amount of protein could be calculated. In Holland this was not practical, and from a large number of different determinations of various substances in blood and plasma we concluded that the volume was not greatly altered. In view of the qualitative change in protein that we found in Holland, we tried in Germany to obtain data on the electrophoretic constitution of the protein but with great difficulty. A few samples of serum from cases of famine oedema in Germany were flown to Oxford and examined in the ultra-centrifuge by Dr. Ogston without any abnormality being discovered.

Professor Himsworth's suggestion that there may be a failure of destruction of antidiuretic hormone is very interesting, but I think it is unlikely as there is usually no evidence of liver damage and it is unlikely that such damage occurred within seven days in Dr. Dicker's rats. But an increase in the amount of antidiuretic hormone in the circulation is the most probable hypothesis to explain the increased reabsorption of water and salt in the renal tubules.

during dry weather. Thus during a few months they often come in contact with fly and the disease becomes noticeable after their return to their normal grazing grounds many miles away from tsetse. Here the disease is transmitted from animal to animal by *Stomoxys* and other biting flies. It is in these cases where a prophylactic drug which would protect the animals during their dry-weather grazing and contact with the fly would be most valuable. Such a drug is within the bounds of possibility, but when a chemical is required which will protect animals indefinitely in these tsetse areas the realms of practicability are exceeded at any rate for the present.

Other methods by which cattle become infected are contact with fly during travel from one part of the country to another on ordinary trade routes. Providing the fly belt through which they pass is not too extensive, an injection of Phenanthridinium 1553 or some other drug which will protect for a few days should prove a practical proposition and confer protection for the short period of risk from tsetse. On many occasions cattle are trekked through a fly belt at night, but this is often a hazardous undertaking and in any case is not effective as several species of *Glossina* feed at dusk.

Leaving the tsetse fly aside, a vast amount of trypanosomiasis in cattle is represented by *T. congolense* infections in herds far removed from known tsetse infestation. This is usually a chronic infection, causing unthriftiness and gradual emaciation, with exacerbations of virulence at certain times of the year. Sometimes these occur during drought when the animals are in poor condition owing to lack of grazing. At other times they occur during the rainy season when the biting flies such as *S. hematopota* and *Tabanus* occur in large numbers and the animals' resistance is reduced by fly worry, and mechanical transmission takes place more easily. Normally the disease in these non-tsetse areas spreads through a herd fairly slowly, which is in very marked contra-distinction to what happens if the herd is exposed to tsetse. In these non-tsetse areas there is no doubt that special conditions are involved and these occur in nature but are extremely difficult to reproduce under artificial conditions. In spite of numerous attempts to transmit *T. congolense* mechanically by *Stomoxys* and the *Tabanidæ* over a period of many years at Entebbe veterinary laboratory in Uganda I have always failed to set up infection, and under laboratory conditions where cattle are kept housed even if fairly large numbers of biting flies are present, cross-infection rarely if ever takes place. Over a period of sixteen years with trypanosome infections constantly being maintained in cattle I have yet to see an accidental infection taking place, and I cannot imagine that cross-infection by mechanical means could ever happen in this country under laboratory conditions, or even in ordinary farm buildings.

Mechanical transmission in human beings rarely occurs, but in the outbreak of sleeping sickness in Mwanza, Tanganyika, about twenty years ago, Duke was under the impression that mechanical transmission by tsetse actually took place in the villages where the fly concentration was extremely heavy.

I have not touched upon the epidemiology in other animals than cattle. Trypanosomiasis in dogs, sheep, goats and horses is almost invariably by the bite of a tsetse, and mechanical transmission does not appear to be an important factor. Dogs are especially susceptible to trypanosomiasis, and *T. brucei* and *T. congolense* are the important parasites. The disease set up by *T. brucei* and *T. rhodesiense* is indistinguishable on clinical grounds and is invariably a severe infection. Dogs are a very sensitive index of the presence of tsetse in a particular area.

Dr. Cecil A. Hoare (Wellcome Laboratories of Tropical Medicine, London): *Reservoir hosts of human trypanosomiasis*.—The trypanosomiasis affecting man and domestic animals afford one of the best examples of a field where the medical and veterinary sciences meet on common ground. The contact is particularly close in the sphere of epidemiology, especially in Africa where the tsetse flies and wild game represent a common pool for the pathogenic mammalian trypanosomes.

environmental factor such as famine intervenes, no epidemic occurs. If my memory serves me aright it was a famine which precipitated the devastating epidemic in Uganda early in this century.

I have already pointed out that domestic animals and tsetse fly are incompatible and in areas infested with *G. morsitans*, *G. pallidipes* and most of the other non-riverine species of tsetse flies, domestic animals cannot survive. In areas infested with *G. palpalis*, such as river banks and the Lake shore, cattle can exist and even thrive, at any rate in Uganda. This is mainly due to the fact that *G. palpalis* does not transmit *T. congolense*, which is the most pathogenic trypanosome as far as domestic animals are concerned. It does, however, transmit *T. vivax* and *T. brucei* but neither of these parasites causes severe disease, at any rate when transmitted by *G. palpalis*, in animals kept in good environmental conditions. Under adverse conditions such as drought, long journeys, work as draft oxen, &c., this tolerance to *T. vivax* and *T. brucei* breaks down, and a severe disease supervenes. An interesting epidemiological point arises in connexion with *T. brucei* for it has been seen that this organism can on occasion set up a severe disease in cattle when transmitted by *G. morsitans* or *G. pallidipes*.

Treatment of cattle which are in constant contact with tsetse fly is of little value owing to the fact that reinfection is taking place. When herds treated by the modern drugs for *T. congolense* repeatedly break down after treatment this indicates almost invariably that reinfection is taking place through tsetse. On more than one occasion this fact has led to a sustained search and the tsetse hitherto considered to be absent have been discovered. Parts of Uganda and Zanzibar are cases in point.

One of the most important factors in the epidemiology of trypanosomiasis whether it be of man or animals, is the shifting fly population. The "fly" areas, apart from those infested by *G. palpalis* near lakes and rivers, are never static and in recent years *G. pallidipes* and to a certain extent *G. morsitans*, have spread alarmingly. In Uganda where I have had first-hand experience over many years, the extension of the fly areas during the past three or four years has been most serious and in large areas the cattle population has been exterminated. It has been suggested that the fly *G. pallidipes* existed in these areas all the time and has only now been discovered. I can say categorically that as far as Uganda is concerned this is not so, because for many years large herds of cattle occupied these regions and healthy cattle are the best indicator that tsetse does not exist. In one particular area in Buruli in the province of Buganda there were famous grazing grounds early in this century, but *G. morsitans* and probably *G. pallidipes* invaded the area and existed in large numbers prior to the rinderpest epidemic about 1918 which killed off the big game, especially the buffalo. The fly disappeared and the cattle returned and thrived, and I myself carried out a careful survey using bait animals in 1928. No tsetse were to be found. Within the last three years this same country has become reinfested, probably by traffic across a narrow strip of water, from a recognized "fly" area and the cattle have again been wiped out—that is twice within forty-odd years, due to shifting fly population.

There is no doubt that tsetse flies feed on game and that game, especially buffalo and antelopes, carry trypanosomes which are pathogenic to domestic animals. There is also no doubt that buffalo and to a certain extent elephants, can and do carry tsetse, especially *G. morsitans* and *G. pallidipes*, many miles into fresh country which if suitable may become permanently infested and the cattle population infected with trypanosomiasis. The question of game destruction is outside the scope of this discussion but from the epidemiological point of view it has been observed that with the disappearance of game the fly has gone and trypanosomiasis of cattle does not occur. Several examples of this can be given from various parts of Africa.

The vast majority of chronic trypanosomiasis in cattle occurs outside tsetse areas and infection comes about in a variety of ways. In some parts of Africa, especially in Nigeria, the nomadic tribesmen move their cattle in search of grazing and water

would gradually adapt itself to the new host, at first behaving like *T. rhodesiense* and subsequently like *T. gambiense*. Conversely, it is thought that after passages through lower mammals the human trypanosomes may revert to *T. brucei*.

However, these views cannot be accepted unreservedly. First, because in enzootic areas of *T. brucei* no cases of human infection have ever been recorded. Secondly, because practically all attempts to infect human volunteers with *T. brucei* have failed. Finally, it has been demonstrated that after cyclical transmission through ruminants for many years *T. rhodesiense* does not lose its power to infect man again, i.e. it does not revert to *T. brucei*.

From these conflicting data it can be concluded that *T. brucei* does not readily adapt itself to man and that its transformation into *T. rhodesiense* does not take place under normal conditions, but presumably this evolution has actually happened in the past and might recur under exceptionally favourable conditions, the nature of which is not yet clear.

We now turn to the question regarding the reservoir hosts of American human trypanosomiasis, or Chagas' disease. Here the role of lower mammals as sources of human infection is much clearer, for in various countries of the New World numerous wild and domestic mammals are naturally infected with *T. cruzi*. This fact is of considerable importance in the epidemiology of human trypanosomiasis. The occurrence of natural infections in wild animals is closely correlated with the incidence of *T. cruzi* among Reduviid vectors. Infected bugs are encountered throughout the Americas, not only in localities where the human disease is endemic, but also outside these areas, where they inhabit the burrows of wild mammals and transmit the infection to these animals.

Since Chagas' disease has a restricted geographical distribution and its incidence in man is very low as compared with the incidence of infection among wild mammals and Reduviid bugs, there can be no doubt that *T. cruzi* is a natural parasite of these animals and Chagas' disease is a typical zoonosis, i.e. primarily an infection of wild animals which act as reservoir hosts from which the disease is occasionally spread to man by bugs introduced into human dwellings. This connexion has been clearly established in South America, where armadillos represent the source of human infection outside human habitations, but once established in a community the infection is transmitted from man to man by the domesticated bugs. Under these conditions domestic animals, like dogs and cats, also acquire the infection and constitute important reservoirs of the disease. The position in the southern parts of the United States is peculiar, for human trypanosomiasis has not hitherto been recorded there, in spite of the fact that local wood rats and Reduviid bugs harbour *T. cruzi* which is capable of infecting man under experimental conditions.

In conclusion, it may be noted that, in addition to trypanosomes which are common to man and lower mammals, there are a number of cases on record showing that purely animal parasites, e.g. *T. vivax* and *T. lewisi*, can occasionally break the barrier of host-restriction and establish themselves temporarily in man.

Dr. J. T. Edwards stressed the important difference between the human and veterinary aspects in so far as, in the former, two closely related species only, namely *T. gambiense* and *T. rhodesiense* were in question, at any rate in Africa (with *T. cruzi*, of minor importance, in South America), whereas, in the latter, the field was far more extensive and comprised trypanosomes belonging to the three very different groups, namely (a) the *brucei-pecaudi*, (b) *congolense-dimorphon*, and (c) *cazalboui-vivax*. Each of these three groups represented trypanosomes with marked morphological, developmental, and antigenic differences, as well as of response to chemotherapeutic agents, so that in devising methods of control of infection the veterinarian, over a large part of Africa, was presented with a far more complicated problem than the medical worker. If the recent work of Fiennes was confirmed, which pointed to a dermal pathogenesis in *congolense* infection in cattle, with remote disorganization

I propose to restrict myself to the animal reservoirs of human trypanosomiasis. In the case of sleeping sickness we have to deal with two forms of the disease, the chronic and the acute; however, there is no doubt that the causative organisms are very closely related and probably identical, *T. rhodesiense* representing merely a virulent strain or race of *T. gambiense*. Indeed there are indications that the two trypanosomes are convertible into each other.

The question regarding the reservoir hosts of sleeping sickness is highly controversial. In endemic areas of this disease natural infections with trypanosomes of the *brucei* group are common in tsetse flies and among wild and domestic mammals. In view of the absence of morphological distinctions between the three members of this group their identity in natural infections can be established with certainty only by observing their effect in susceptible animals, by inoculating these with the blood of the natural host, by allowing wild tsetse flies to feed on them, or by experimental infection of human volunteers. However, in most cases the nature of the trypanosomes detected in natural infections is determined from evidence provided by the epidemiological data. Thus, trypanosomes found in animals from localities where the human disease is unknown most probably are *T. brucei*, while those occurring in endemic areas of the Rhodesian disease may be either *T. rhodesiense* or *T. brucei*. Since both these species are highly virulent for laboratory animals they can only be differentiated by inoculating human volunteers. In endemic areas of the Gambian disease the differential diagnosis of *T. brucei* and *T. gambiense* is based on the relative virulence of the trypanosome for laboratory rodents.

The occurrence of natural infections with human trypanosomes among wild and domestic mammals has an important bearing on their role as reservoir hosts of sleeping sickness. Significant results, throwing light on this problem, have been obtained from experimental infections of various animals. These have shown that *T. rhodesiense* and *T. gambiense* can be maintained by cyclical transmission through wild and domestic mammals for several years, without losing their transmissibility to man.

From these observations it is concluded that in sleeping sickness, in addition to man, various other mammals constitute a source of infection. The relative importance of the human and animal reservoirs differs according to the type and distribution of the disease. The Rhodesian disease, which is usually encountered on the fringes of thinly populated bush-country abounding in big game, is transmitted by tsetse flies from man to antelopes and from these back to man, antelopes representing important reservoir hosts even in localities which have been depopulated for some years. In the Gambian disease, which occurs in relatively well-populated localities with a sparse mammalian fauna, man appears to be the essential host, but in view of the prolonged survival of the trypanosome in antelopes and domestic animals, without loss of cyclical transmissibility to man, some of these animals should be regarded as potential reservoir hosts.

The question of reservoir hosts of *T. gambiense* and *T. rhodesiense* is closely linked with that of their relationship to *T. brucei*, which has both a theoretical and practical interest, for there are reasons to believe that the human trypanosomes have originated from *T. brucei*. This question has also an important bearing on the epidemiology of sleeping sickness, for if it could be proved that *T. brucei* is capable of establishing itself in man, both wild and domestic animals harbouring this trypanosome would have to be reckoned with as dangerous sources of human infection. However, there is considerable controversy on this matter. The chief factor which prevents *T. brucei* from gaining a footing in man is the trypanocidal action upon it of normal human serum, to which the human trypanosomes are resistant. But it is conceivable that persons suffering from pathological conditions which destroy the trypanocidal power of their serum might become susceptible to infection with *T. brucei*. Furthermore, exceptionally virulent strains of this trypanosome might overcome the trypanocidal action of normal human serum. Having thus established itself in man *T. brucei*

fixation test. This proved the very close antigenic affinity existing between the several members of the *brucei-pecaudi* group. However, although ordinarily it is not possible to transmit *T. equiperdum* to rats, yet, very rarely indeed, a strain from a natural case can be discovered to infect an animal of this species, and when once that has been achieved then serial transfer in the species takes place readily, and the disease-picture is indistinguishable from that seen after *T. brucei* or *evansi* infection in them.

To the veterinarian, the principles of epidemiological control in tropical or sub-tropical territories as applicable to a grave disease, like, for example, cattle plague, differ enormously from those applicable to the trypanosomiasis. For, whereas, in the former, resort must be had to vaccination (and research undertaken continuously to perfect methods of vaccination), in the latter resort must be had to chemotherapy (also with the steady pursuit of improving methods of both preventive and therapeutic treatment). In the case of the former, methods of segregation and quarantine are usually out of the question. In the case of the latter, however, the recent discovery of excellent insecticides, such as D.D.T., will supplement, if not eventually supplant, chemotherapy.

Brigadier J. S. K. Boyd said he thought Dr. Carmichael was taking an unduly pessimistic outlook on the subject of drug prophylaxis in animal trypanosomiasis. In the Belgian Congo, van Hoof and his colleagues had reported that a single dose of pentamidine protected man against infection with *T. gambiense* for a period of six months. It seemed reasonable to hope that a drug conferring a similar or even a greater degree of protection against *congolense* infection might some day be discovered. Recent reports on certain phenanthridinium compounds were encouraging and it was possible that sooner or later a drug, possibly less toxic than those already known, and conferring a longer period of protection, might be discovered.

Dr. E. M. Lourie (Director of the Warrington Yorke Department of Chemotherapy, Liverpool School of Tropical Medicine) supported Brigadier Boyd's optimism in regard to the possibility of eventually finding an effective prophylactic agent for *T. congolense* infections of cattle. All that would be needed, after all, would be to find a substance which is not only lethal to the trypanosome but which is also capable of being retained in the host, in adequate amount, for a long period of time. There should be no insuperable difficulty in finding a compound in which these two properties are combined, and there is every reason to expect that substances of such a nature will become available before very long.

Dr. Lourie remarked that many of the problems of trypanosomiasis have been made more puzzling because of a tendency to regard the characters of *T. gambiense*, *T. rhodesiense*, *T. brucei*, &c., as of a fixed nature. One must constantly bear in mind, however, that the characteristics of any particular strain of trypanosome can undergo radical changes, which may be retained for very long periods. For example, after passage through suckling rats, *T. gambiense* no longer produces the chronic benign infections ordinarily characteristic of *T. gambiense* in laboratory animals; it acquires the virulent properties, together with other features, of *T. brucei* (Sandground, *Ann. Trop. Med. Parasitol.*, 1947, **41**, 293). Is it not possible that the reverse change, that is from virulence to benignancy, may account for the situation in Uganda, referred to by Dr. Hoare? After the devastating epidemics on the shores and islands of Lake Victoria at the beginning of this century the populations were shifted from the affected areas. On their return, many years later, there was no recurrence of epidemic conditions, although Fairbairn and Burt (*Ann. Trop. Med. Parasitol.*, 1946, **40**, 270) have shown that trypanosomes may retain their infectivity after many years of passage through game animals, which are, of course, abundant on the shores and the islands of Lake Victoria. However, a highly significant point is that although infectivity for man is retained after many years of passage through other animals, it is not unlikely that virulence for man may be considerably reduced. Indeed, Fairbairn and Burt produced evidence for such a change in a strain of *T. rhodesiense*

of the internal tissues, especially the thyroids, resulting from the products of the superficial infection, then the whole conception underlying chemotherapeutic treatment would need to be revised. So far, in trypanosome control, with the extreme difficulty of dealing effectively with vectors and carriers, main reliance had had to be placed on diagnostic methods coupled with chemotherapeutic procedures. Dr. Edwards himself, after experiences in India and Egypt (and the same applied to North African territories generally) had been concerned only with trypanosomiasis caused by that monomorphic, mechanically-transmitted trypanosome of the *brucei-pecaudi* group known as *T. evansi*. What was striking in connexion with it was the difference in response of the different species of domestic animal to chemotherapeutic treatment. Since the introduction of Naganol (Bayer 205) towards 1923 the prospects of recovery after proper treatment had changed greatly for the better. Moreover, preventive treatment was hopeful, for after injection of a prophylactic dose the drug remained in trypanocidal concentration in the system for over a month. In therapeutic treatment, the response was paralleled by the susceptibility of the species. In horses, which were very highly susceptible, nothing was effective save Naganol, administered intravenously in adequately large doses, repeated at monthly intervals, on two or three occasions, preferably concurrently with intrathecal administration to ward off possibility of a trypanosomal cerebrospinal meningitis (as Naganol did not traverse the "blood-brain barrier"). Whereas in ordinary cattle and buffaloes, among which outbreaks occasionally arose caused by strains of the trypanosome particularly highly adapted to these relatively resistant species, much less drastic treatment, using simpler remedies, was usually fully effective, the tissues of these animals being able to fend, as it were, for themselves after a little help. In these more resistant species, however, the trypanosomes could be shown to persist, without causing obvious harm to the hosts, after incomplete treatment—a status which could not be established in the far more highly susceptible equine. That Indian Zebu cattle could constitute dangerous reservoirs of infection was exemplified in the classic outbreak in Mauritius over half a century ago, when the local cattle were decimated after the importation of some Indian cattle. Between horses and cattle, in susceptibility and response to chemotherapy, came dogs and camels, among which *T. evansi* infection constituted a grave menace in the extensive territories with which the speaker was familiar. In dogs, intravenous Naganol therapy had promptly suppressed local outbreaks, as in foxhounds, while in camels, improved methods of diagnosis, such as the mercuric-chloride gel test, for those chronic infections in which the trypanosome was not readily detectable, coupled with Naganol therapy had proved wholly satisfactory.

Whether *T. gambiense* and *T. rhodesiense* of man and *T. brucei* of animals were so nearly related that human infection could arise through adaptation of the animal trypanosome, by some process not yet discovered, to human beings was a point of very grave epidemiological importance. The experiments of Kleine and others on human volunteers failed to support the assumption that adaptation took place. However, veterinary experience suggested it was not improbable that in natural circumstances such a phenomenon might arise. Thus, for example, effective control of dourine in horses, caused by a trypanosome of the *brucei-pecaudi* group (*T. equiperdum*), transmitted by coitus, had been achieved by wholesale slaughter of carriers detected by the application of the complement-fixation test on the blood serum. The antigen used in the test consisted of a fresh suspension of trypanosomes separated from the blood of small laboratory rodents (rats or mice) suffering from a rapidly progressive hyperacute septicæmia following inoculation with highly adapted strains of *T. brucei* or *T. evansi*. These trypanosomes, and not *T. equiperdum*, were employed because it was extremely difficult to discover a strain of *T. equiperdum* from natural cases that was infective for these rodents, but experience proved that antigen prepared from *brucei* or *evansi* strains was fully satisfactory in the complement-

Section of Anæsthetics

President—JOHN CHALLIS

[April 2, 1948]¹

d-Tubocurarine Chloride

By T. CECIL GRAY, M.D., D.A.

Two years ago we (Gray and Halton, 1946) expressed the opinion that *d*-tubocurarine chloride was the curare preparation of choice and were surprised that anæsthesiologists of the United States had preferred a comparatively crude substance. It is gratifying to find that the pure alkaloid is now used almost exclusively in this country and tends to replace intocostin in the New World. It is unfortunate, however, that the States continue to assay their preparations against an arbitrary standard rather than compute the dosage in mg. of the pure alkaloid. It is even more regrettable and to be deprecated that one firm has introduced a preparation of tubocurarine of different strength to that usual in this country. Such deviations from accepted local custom can only cause confusion and may be dangerous.

The history, pharmacology and story of the clinical use of *d*-tubocurarine chloride have been amply discussed during the last years. This paper, therefore, will be a critical appraisal of the status of this substance in the light of three years' experience of its use in anæsthesia.

I circulated a questionnaire to all the anæsthetists in the Liverpool district who were using *d*-tubocurarine chloride for their major abdominal and thoracic surgery. From the replies it would appear that in Liverpool alone close on 8,500 cases had been anæsthetized with the aid of this substance up to the end of 1947. Much information accrued from this survey, and, most important, it was evident not one of these other anæsthetists had had a single death which they attributed in any way to *d*-tubocurarine chloride. Nor had they seen any evidence of an unexpected side-effect.

From my own observations on the human electrocardiogram and from animal experimentation (Gray and Gregory, 1948) it seems quite certain that there is no significant effect produced by *d*-tubocurarine chloride on the heart. In animals large amounts injected quickly may produce a sudden fall in blood-pressure. In human subjects, although Harroun and her colleagues (1947) have described a slight fall in blood-pressure, I have never been able to observe this and in two cases it did not follow the very rapid injection of doses of the order of 45 mg. Nor did Smith (1947), in the experiment in which he received 500 units of intocostin, exhibit any alteration in the blood-pressure.

There has not been any evidence of kidney or liver dysfunction following the use of tubocurarine nor, in my experience, has there been any hyperglycæmia. I have used this substance in diabetic patients without any disturbance of their carbohydrate balance.

¹ The March Meeting will appear in the next issue of the *Proceedings*.

maintained for many years in sheep, although it is true they found no such evidence after passage of the same strain through antelope. However, these workers are precluded from making complete studies of virulence in man, because of the necessity of curing their volunteers at a very early stage of infection. Is it, then, not possible that the strains which produced the serious Uganda epidemics at the turn of the century may have subsequently become benign and relatively unimportant during their sojourn in game animals, before human resettlement was allowed in the affected areas?

No doubt many of the epidemiological problems of trypanosomiasis require that we should disabuse ourselves of the notion that *T. gambiense* always behaves in such and such a way, *T. rhodesiense* in another way, and *T. brucei* in still another way.

Dr. F. Hawking pointed out that most of the trypanosomes which infected cattle in Africa were derived from wild game, and so were some of those which infected man. Control of game was necessary for the control of trypanosomiasis; but this did not mean destruction of the game, since ample game reserves could be set aside for their preservation.

Dr. P. L. LeRoux: No mention has been made of the possible influence which temperature may have on the epidemiology of trypanosomiasis. In the case of human trypanosomiasis in Northern and Southern Rhodesia and in the Bechuanaland Protectorate, it is significant that the disease seems to remain confined to certain well-defined areas—Lake Tanganyika and the Luangwa Valley in Northern Rhodesia, certain parts of the Zambesi Valley in Southern Rhodesia, and the endemic area in Northern Bechuanaland—which are probably the hottest areas in these territories. It has been reported from Tanganyika that the incubation of the pupæ of *Glossina* has resulted in more flies becoming infected, on exposure to an infected meal, than is otherwise the case.

It would appear that temperature, in the case of human trypanosomiasis, must have a direct influence on the development of the trypanosome in the tsetse fly and this may explain why cases do not occur in the rest of the *Glossina*-infected areas.

The destruction of game for the eradication of the tsetse fly seems necessary and the complete disappearance of the "fly" from the Northern Transvaal after the outbreak of rinderpest, is often cited in support of game destruction. In the case of the Transvaal the "fly" was actually on the decrease before the rinderpest invaded the country and the rinderpest did not kill off all the species of antelopes. The zebra is not susceptible to rinderpest.

It would appear, also, that other tropical diseases of man and stock are directly influenced by temperature in that the development of their parasites or viruses in the invertebrate hosts is more dependent on temperature than is generally realized or accepted.

Dr. C. A. Hoare (in reply): While the finding of *T. congolense* in India is an isolated case, in *T. vivax* we have an example of a tsetse-borne infection which had spread outside its natural boundaries to Mauritius, the West Indies and South America, where the disease is transmitted to cattle mechanically by horse-flies. As regards surra, the disease occurs all along the Mediterranean coast of North Africa, from Egypt to and including Morocco, where it is represented by races affecting camels and equines. The existence of common antigens in trypanosomes of the *brucei* group has been demonstrated recently by van Hoof, who has shown that immune serum of one of these trypanosomes, when added to the culture medium, inhibits the growth of the others. Recent work by Brand and Johnson indicates that the metabolic processes of trypanosomes belonging to various groups show marked differences which may be correlated with differences in their response to chemotherapeutic agents. With regard to the relationship between *T. gambiense* and *T. rhodesiense*, the clinical manifestations attributed to these parasites are not clearly demarcated, for cases showing symptoms of one type of sleeping sickness may occur in a minority within the area of distribution of the other type.

that provided by laparotomy, tightening of the diaphragm and intercostal muscles in association with bronchospasm is likely to occur. I am convinced that this accounts for most of the difficulties which have been experienced. The whole picture in such a case is changed by increasing the depth of anæsthesia or by further curarization. I feel justified in saying that the possibility of this complication need be no deterrent in the use of d-tubocurarine chloride.

As to the effects on other smooth muscles, Cole (1946) has shown in dogs that tubocurarine abolishes the normal intestinal movements and that they are restored by morphine. Massey Dawkins (1947) reported a series of cases in which the incidence of post-operative ileus caused some inconvenience.

In man the intestinal movements are still very evident after tubocurarine. It is a feature of these anæsthetics that the colon and even the ureters exhibit active peristalsis and neither I nor any of those answering my questionnaire have seen any increased incidence of ileus following its use. If tubocurarine itself really caused ileus we might expect to see this complication a little more often in thoracic work where large doses are often employed. We have not had a single case.

Idiosyncrasy.—The factors determining the dosage of d-tubocurarine chloride are the patient's age, physique, general condition, and in children, body-weight. To some extent possibly the anæsthetic agent with which it is going to be used should be considered. A factor of some interest, but less well recognized, is that if patients have a high natural or acquired tolerance to sedative drugs, notably morphine, they are likely to require more d-tubocurarine chloride to produce the desired response. Even, however, when we take all these factors into consideration there seems to be a variability in patients' reactions. Out of the 15 observers who answered my questionnaire this variation was mentioned specifically by 12. In the vast majority of the cases it is so slight as to be of little or no clinical importance, but on occasion it has been extreme. Halton and I (1948) have recently described two cases of apparent idiosyncrasy and we had ample opportunity of confirming the hypersensitivity of the second case as she underwent a three-stage operation and her reactions to the drug were identical on the three occasions.

Now there are those who would say there is no such thing as idiosyncrasy to a drug. All I wish to relate here is that some patients show an exaggerated and a dangerous response to injections of d-tubocurarine chloride which, if not anticipated, may place the anæsthetist in an embarrassing and difficult position. For these reasons we advocate very strongly that to be safe, all who use this substance should administer a preliminary small dose as a test. It does not matter whether the patient is anæsthetized or not when this test dose is given. The effects on the respiration will be apparent in either case.

In a final attempt to evaluate the dangers of this agent, I investigated the cases which had been reported to the coroner in the Liverpool area from April 1945 to December 1947, the period during which d-tubocurarine chloride has been most widely used. There have been 18 fatalities following the use of this drug within forty-eight hours of operation. The details of these deaths are analysed in the table. Within the same period 60 patients died following the use of other anæsthetics and 28 of these fatalities were due to mismanagement of the anæsthesia. Owing to the difficulty of obtaining any accurate estimate of the total number of non-curare anæsthetics given in this large area it is impossible to express these latter figures in percentages. However it should be noted that the majority of the major general surgery and all the major thoracic procedures have been performed using d-tubocurarine chloride. Furthermore those deaths which were due to mismanagement of the anæsthesia in the non-curare cases were often extremely disturbing. In only one case which had died following d-tubocurarine chloride was there a really grave

Therefore, it is in a sense true to say that this is one of the least toxic drugs used in anaesthesia. Those stumbling-blocks, the heart, the liver and the kidneys, are unaffected by it. Nevertheless, it is potentially one of the most dangerous drugs we are called upon to exhibit.

d-Tubocurarine chloride produces paralysis of striated muscle by interfering with the conduction of the motor impulse across the myoneural junction. The muscles of respiration, the intercostals and diaphragm, being striated, are affected. Although some muscles are affected more and therefore earlier than others there is really no constant serial progression in the paralytic effects. There is a marked overlap and any dose likely to be of service to anaesthetists will affect to some extent the respiratory muscles. At the outset, therefore, it might be said that any substance which is likely to impair the respiratory function so drastically cannot be safe. That is a matter of opinion, for it is now recognized that the anaesthetist is able to compensate for such effects and restore to normal the impaired tidal exchange. That is now an everyday procedure but complete competence in assisting respiration and in dealing if necessary with an apnoeic patient is an essential pre-requisite for the anaesthetist who intends to use this substance.

Ever since the important work of Ranyard West in 1938 there has been reason to fear that bronchospasm might prove to be a serious if not a prohibitive factor in the employment of preparations of curare in clinical practice. West examined the exposed lungs of guinea-pigs and observed that an intense bronchiolar-constriction followed the intravenous injection of crude extracts. His clinical experiences also seemed to confirm this action.

There appeared to be a certain similarity of this action to the effects of injections of histamine, a similarity which was made more striking by the report of Comroe and Dripps (1946) that the intradermal injection of tubocurarine produced a wheal similar to that produced by histamine. Landmesser (1947) in an important communication last year showed that bronchiolar-constriction occurred in seven out of ten dogs after an injection of 0.3 mg. of *d*-tubocurarine chloride. The spasm did not occur if the animal was "protected" by the previous administration of the anti-histamine preparation, benadryl. The work of Gregory and Schild (1947) has shown quite conclusively that histamine is liberated when solutions containing *d*-tubocurarine chloride are perfused through mammalian skeletal muscle.

In April 1947 when this Society discussed this subject (*Proc. R. Soc. Med.*, 1947, 40, 593) more than one reputable authority reported bronchospasm in patients anaesthetized with *d*-tubocurarine chloride and in one or two cases this was thought to have produced a fatal result. We should review the position in regard to this possibility, remembering, however, not to give undue importance to the results of animal experiments when, as is in fact the case, the clinical evidence contradicts them. Halton and I have given *d*-tubocurarine chloride to 2,500 cases; out of these broncho-constriction has occurred only once and that was in a very bad asthmatic who was bronchoscoped when thiopentone was the anaesthetic agent used. The only other report of bronchospasm in Liverpool also followed a bronchoscopy when difficulty was experienced in inflating the lungs after withdrawal of the bronchoscope. Bronchospasm is not uncommon when bronchoscopy is performed under thiopentone, and in this latter case anoxia was present before the spasm developed and was an aggravating feature. Therefore, there have been two cases in over 8,000, and they both might have been expected to develop this complication. When there is a resistance to manual inflation of the lungs by pressure on the rebreathing bag, quite apart from occasions when there has been frank obstruction due, for example, to a kinked tube, there is a tendency for anaesthetists to say, "Ah! bronchospasm". The condition has been described by Morton (1945) as characteristic of light anaesthesia and this I believe it to be. If the anaesthesia is too light, whenever there is an intense stimulus such as

curarine is given intravenously and our custom is to give $\frac{1}{2}$ of the estimated induction dose as a test. Usually for adults this is 5 mg., and the effect of this on the conscious patient is watched for two minutes. In the very great majority the result is purely subjective. They feel a little drowsy and heavy in the eyelids, which they will frequently close. On request they are able to open their eyes and there should be no real ptosis. Any patient who exhibits more than this, e.g. complete ptosis, difficulty with speech or any difficulty with respiration is considered as being hypersensitive. This gives us a nice indication of the likely requirements of patients, particularly aged patients, in regard to d-tubocurarine chloride.

In the absence of any unforeseen reaction another 10 mg. is given followed immediately by 0.5 gramme of thiopentone. An endotracheal tube or a pharyngeal airway, depending upon the exigencies of the case, is introduced and the cheeks packed to ensure a close fit of the mask which is now applied and connected to a closed circuit anaesthetic machine. Anaesthesia for abdominal cases is usually maintained with thiopentone or kemithal, 50% nitrous oxide and a little ether if required, the tubocurarine being given in doses of 5 mg. as necessary. I consider that the best attitude to the question of ether-d-tubocurarine chloride potentiation is to use the same amount of tubocurarine which we know to be non-toxic and to reduce considerably the amount of toxic ether. For some cases cyclopropane is preferred particularly in those who are aged, shocked or have a poor myocardial reserve.

In thoracic work anaesthesia is maintained with kemithal and 30%-50% nitrous oxide and oxygen. The average order of dosage in, for example, an adult undergoing pneumonectomy would be thiopentone 0.5 gramme, kemithal 0.5 gramme or less and 30-35 mg. of d-tubocurarine chloride.

There are some further points about this technique: First and most important is the necessity to aid or assist the respiration when d-tubocurarine chloride has been given. Any dose which produces abdominal relaxation depresses the respiration to some extent. It is easy to show that even an injection of 15 mg. of d-tubocurarine chloride materially reduces the tidal volume and causes a collapse of the chest wall.

Now unless the anaesthetist compensates for these effects during the operation he must be prepared to have not only the troubles attendant upon under-ventilation at the time of the operation, but also a high incidence of post-operative pulmonary collapse. I have repeatedly seen experienced anaesthetists returning patients to the ward after operation still partially curarized. They often appear to be breathing fairly adequately and to be of a reasonably good colour; but a little closer observation would show that their respirations are depressed and inadequate. It is my opinion that nothing will so predispose to chest complications as returning patients to the ward in this condition. Harroun *et al.* (1947) have shown that in dogs post-operative atelectasis always follows the administration of tubocurarine if the animal is returned to his cage before his intercostals have fully recovered. The dog appears fit and has a fair respiratory exchange but the collapse is inevitable. It is so easy to give a dose of prostigmine and atropine, and in order to be quite certain it is now almost my invariable custom to do so. This injection of prostigmine should have the same sedative effect on anaesthetists as do the "hypnotic sutures" of Moynihan on surgeons. From the tracing in fig. 1 it will be seen that prostigmine will increase the tidal exchange even twenty-three minutes after an injection of thiopentone 0.5 gramme and tubocurarine 15 mg.

It will be noticed that in the technique I have described the d-tubocurarine chloride is administered before the induction of anaesthesia. There is a clear rationale for this. The intravenous injection of thiopentone is effective within seconds, that of d-tubocurarine chloride takes about two minutes to reach its maximum effect. Synchronizing the maximum effects of both these drugs by giving the tubocurarine first facili-

TABLE I.—DEATHS REPORTED TO THE CORONER FOLLOWING D-TUBOCURARINE CHLORIDE 1945-47

Cause of death	Registrars- Residents	Specialists	Total
Mismanagement of anaesthesia ..	3 (0.18%)	3 (0.05%)	6 (0.07%)
Cardiac failure	2 (0.12%)	1 (0.02%)	3 (0.04%)
Shock and hæmorrhage	3 (0.18%)	3 (0.05%)	6 (0.07%)
d-Tubocurarine chloride	0 (0%)	1 (0.02%)	1 (0.01%)
Other causes not relative to anaesthesia	0 (0%)	2 (0.03%)	2 (0.02%)

Number of cases—Residents .. 1,687
Specialists .. 6,646

8,333

Number of deaths reported to Coroner—18, i.e. 0.22%.

fault in technique and whilst the others in the light of subsequent experience with the drug might have been avoided they were bad risks and were due to misjudgment rather than to mismanagement.

The case in which death was attributed to tubocurarine was that of idiosyncrasy which has already been reported (Gray and Halton, 1948). If steps had been taken to avoid the regurgitation of stomach contents even this case might not have ended fatally.

How safe then is this substance? Dr. John Talbot of the University of Buffalo School of Medicine stated recently: "That it is only human to minimize the untoward reactions of a new therapeutic substance in the enthusiasm of discovering and subjecting it to clinical trial" (Talbot, 1948). This mistake I hope I have not made. I have reviewed the facts as we know them and it is for each of us to form our own judgment.

The use of tubocurarine confers two blessings upon the anaesthetists and the surgeons and one, perhaps the greatest, upon the patient. It ensures complete abdominal relaxation, and, if necessary, perfect control of the respiration. Both of these are possible quickly and at once, with a certainty which is most comforting for the anaesthetist and surgeon. The great blessing for the patient is that the anaesthetist can achieve these desiderata without resorting to deep anaesthesia.

We have in the past considered that it served a further function. The small amounts of narcotic drugs necessary to maintain anaesthesia led us to believe that the narcotic effectiveness of anaesthetic agents was increased by d-tubocurarine chloride, i.e. there was a potentiation effect; however, this is not the case. I have carried out a controlled series of experiments in which volunteers have been subjected to repeated doses of thiopentone and d-tubocurarine chloride and have tested their pain sensitivity and the time of their return to consciousness. It has become clear in the course of these experiments that our impression, as may so often be the case with clinical impressions, led us to an unjustifiable assumption. The experiments are still progressing but we have gone far enough to be able to say that there does not appear to be any decrease in sensitivity to painful stimuli or prolongation of the narcosis when d-tubocurarine chloride is used with thiopentone.

TECHNIQUE

Each anaesthetist will adopt the technique which suits him best, but I would again appeal for the universal adoption of a test dose for I fear that otherwise difficulty and embarrassment, if not indeed tragedy, will sooner or later attend the administration of effective doses of this substance. The following technique has given us the most consistent and best results: Very light premedication is still the rule. For adults we use morphine grain 1/6 (11 mg.) and atropine grain 1/100 (0.65 mg.). The tubo-

A further comforting feature is that with this type of anæsthesia the condition of the patient at the end of the operation does not deteriorate when the mask is removed as is so often the case with other methods of anæsthesia, particularly if cyclopropane is used. You see the patient in his worst condition at the end of the operation and not half an hour later in bed in the ward (figs. 2 and 3).

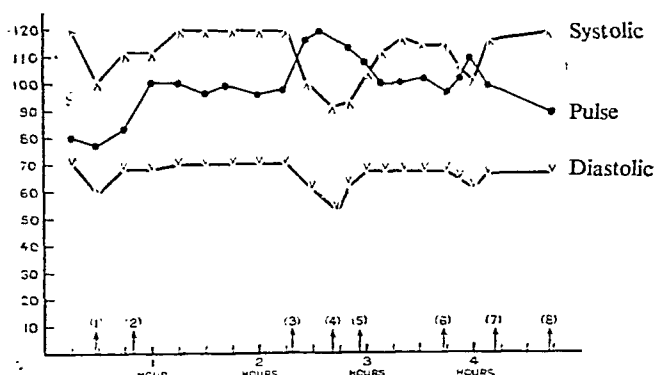


FIG. 2.—B.P. and pulse record of a patient undergoing transthoracic oesophago-gastrectomy. Note: (a) The fall in B.P. at (3). (b) The strong circulatory condition after the close of the operation. (1) Induction. (2) Chest opened. (3) Mesenteric traction. (Anæsthesia too light.) (4) — (5) Rest. (6) Close wound. (7) Return to bed. (8) In bed.

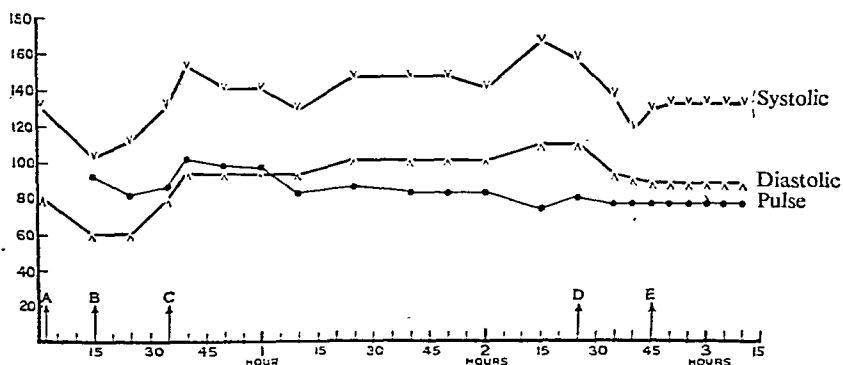


FIG. 3.—B.P. and pulse record of a patient undergoing transthoracic oesophago-gastrectomy. Note the steady blood-pressure after removal of the anæsthetic mask. (A) Induction. (B) Operation started. (C) Pleura opened. (D) Closing up. (E) Anæsthetic completed.

Good post-operative condition of the patients despite bigger and more extensive operations and working with poorer risks is definitely a feature of this type of anæsthesia. We are seeing less shock than ever before. I attribute this to early replacement therapy, replacing the lost blood almost drop for drop, and to light anæsthesia.

(2) *Vomiting*: The actual incidence of vomiting in my own series of abdominal cases has not been significantly altered, but the length of time and severity of this vomiting is very considerably modified. Patients may still return the first drink, especially, as is so often the case, when this is given too early post-operatively, but the prolonged nausea, malaise and vomiting, which used to be seen have practically disappeared from our post-operative wards.

(3) *Pulmonary complications*: With regard to pulmonary complications it is extremely difficult if not impossible to come to any clear and definite conclusion. I have a slide showing figures for pulmonary complications in a series of upper and

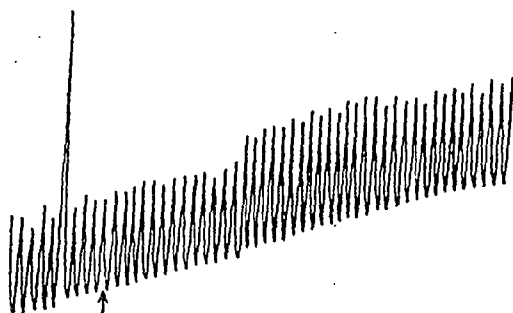


FIG. 1.—Spirometer recording of the respiration of a human subject twenty-three minutes after an intravenous injection of thiopentone 0.5 grammes and tubocurarine 15 mg. At ↑ prostigmine 2.5 mg. and atropine gr. 1/100 was administered intravenously. The increase in tidal volume was evident one minute later.

tates either intubation or the insertion of a pharyngeal airway. Some have reported a difficulty in intubation after thiopentone and tubocurarine; others have had to use more than 15 mg. for this purpose. I feel that if they gave the tubocurarine first they would appreciate the difference and have little difficulty. The objection to this procedure is that the needle may come out of the vein and the patient be left conscious and partially curarized. On the single occasion when this did happen and I felt that I might have difficulty in finding another vein I induced the patient quickly and smoothly with cyclopropane and on inquiry later she reported no unpleasant effects.

Intubation.—I now intubate rather more frequently. I am impressed with the danger of regurgitation of stomach and intestinal contents. The relaxation of the oesophagus and the light anaesthesia conduce to this and it is an accident which will obviously be more likely if there is an element of gastric or intestinal obstruction. Furthermore, in upper abdominal operations when an endotracheal tube has not been passed, manual inflation of the stomach has occasionally been coincidental with inflation of the lungs. This can be very trying for the surgeon and amusing to the onlookers but a little humiliating to the anaesthetist.

RESULTS

In conclusion what are the results likely to follow on the use of this substance? I have employed it in all ages varying from a 4-year old for lobectomy to an old gentleman of 87 who successfully underwent a nephrectomy and ureterectomy. The results have undoubtedly maintained their early promise. This is well exemplified by the fact that out of 145 consecutive lobectomies performed in the Liverpool Chest Surgical Centre there has not been one death. I want to emphasize, however, that the good results are due not to any inherently wonderful properties of d-tubocurarine chloride, but to the use of only light anaesthesia. I would like to examine some aspects of these results in a little detail.

(1) *Shock.*—It is a clinical impression among many that patients who have been anaesthetized with the help of d-tubocurarine chloride suffer less from shock than those who were subjected to deep or moderately deep anaesthesia. Ralph Knight, in America, goes so far as to say that deep anaesthesia is a more potent cause of peripheral circulatory failure than is surgical trauma. There is no doubt that these patients, provided that they have been handled carefully, are on the whole less shocked. Some have even postulated that tubocurarine has an anti-shock action in its own right. There is no pharmacological evidence for this and I do not think that it is a correct observation. The good condition post-operatively of the majority of these patients, I feel convinced, is accounted for by the fact that their vasomotor compensatory mechanisms are still active after a light anaesthesia. Of course, there is likely to be a temporary fall in blood-pressure if the anaesthesia is not adequate when there is stimulation of the deep reflexes either in the abdomen or in the thorax. However, the patient is still able to compensate for these disturbances and quickly recovers (fig. 2).

A further comforting feature is that with this type of anæsthesia the condition of the patient at the end of the operation does not deteriorate when the mask is removed as is so often the case with other methods of anæsthesia, particularly if cyclopropane is used. You see the patient in his worst condition at the end of the operation and not half an hour later in bed in the ward (figs. 2 and 3).

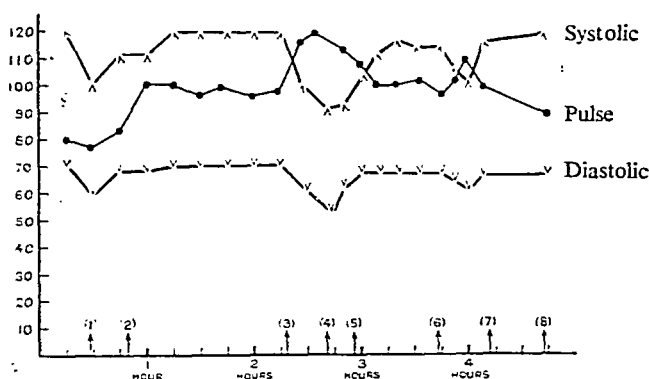


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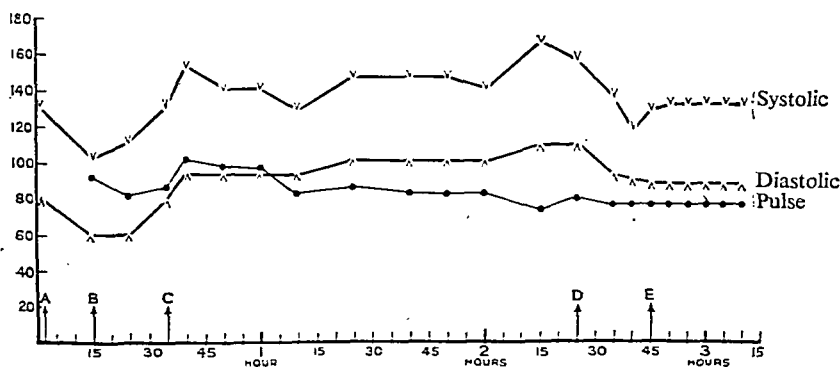


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lower abdominal cases which I personally followed up with great zeal and care, but I consider that figures of these conditions are so misleading and mean so little that I do not intend to show it unless it is specially requested.

The percentage of chest complications which I have recorded in this series is lower by far than my own percentage before the introduction of tubocurarine and considerably lower than most of the reliable reports. Figures are of little value because so much depends upon the criterion of what is and what is not a pre-operative chest complication, on the standard of pre-operative supervision of patients, the season, the climate, and the type of operation.

It is, however, useful to examine the anæsthetic factors accepted as predisposing to pulmonary complications and see how they are affected by the anæsthetic under consideration. Among the most vital of these factors are post-operative depression of the respiration and the cough reflex, prolonged periods of narcosis and immobility with possible respiratory obstruction, and the possible aspiration of vomitus. It is true to say that 90% of our patients who have had d-tubocurarine chloride have their pharyngeal and cough reflexes fully restored at the close of the operation and the majority are co-operative and talking by the time they leave the theatre. The main contributory factors are thereby removed and I do not believe that it is possible to achieve this with certainty in major abdominal and thoracic surgery with any other method of general anæsthesia. The part played by the anæsthetic in causing pulmonary complications must be very materially reduced. I would like to stress once again, however, that if there is one thing worse than returning the patient to bed with a respiration depressed by an anæsthetic agent, it is returning him to bed with his respiration depressed by d-tubocurarine chloride. This will undoubtedly predispose to the incidence of post-operative atelectasis.

(4) *Retention of urine:* There seems to be an increased incidence of post-operative retention of urine. There is, of course, quite a considerable incidence of post-operative retention after any anæsthesia even in those cases in which the operation could have contributed little towards its occurrence. Women are particularly prone to this complication, nervous patients and elderly men with incipient prostatism are also liable to develop it. A series of 127 abdominal cases were reviewed in an attempt to see whether there were any grounds for the complaints. This series did not include those gynaecological or genito-urinary procedures which might be predisposed to urological disturbance. Retention of urine occurred in 24% of these patients and just on 9% recovered after one or more injection of carbachol and 7.9% had to be catheterized. Records of 185 patients were consulted and compared with 137 cases who had not had d-tubocurarine chloride. 15% of those who had been given d-tubocurarine chloride had to have carbachol against only 9% of those who had not had tubocurarine. I think this is a difficulty and I have seen a case following lobectomy in a young male where the patient did not micturate naturally for seven days.

(5) *Difficulty in accommodation:* Lastly there is a tendency to difficulty in accommodation following operation. Four of my cases have complained that they were unable to read a newspaper for forty-eight hours. But I would ask with what other anæsthetic are they likely to try to read a paper so soon after major surgery?

What then is to be our verdict with regard to this substance? I believe that d-tubocurarine chloride is not the final answer, but the absolute certainty of results, its comparative non-toxicity and the ease of the anæsthesia in which it is used are factors which persuade me that, although we have not reached our ultimate goal we have indeed taken a most significant step. Griffith of Montreal observed the softening of electric convulsions by tubocurarine and in a flash of inspired genius saw its application to anæsthesia. He revolutionized our specialty by removing for all time the need for deep anæsthesia.

I would like to express my thanks to all those who have worked with me and contributed so much to the results we have achieved. But very specially must I mention those volunteers who have submitted themselves week after week to anaesthesia and other indignities in the good cause.

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Dr. Frankis Evans said that he had been disappointed in the use of tubocurarine in bronchoscopy, and was interested to learn that Dr. Gray was not using the drug so frequently for this procedure. On the other hand he was most impressed with it in moderate dosage (15 mg.) together with pentothal and cyclopropane for upper abdominal operations.

He had had an interesting experience in regard to the occurrence of ileus after curare. At a certain hospital they had been using for abdominal surgery pentothal 0.5 gramme for induction followed by tubocurarine 10 mg. intravenously with cyclopropane as covering anaesthesia. At the end of the operation the patient was given 1 ampoule (0.5 mg.) of prostigmine intravenously with no buffering atropine. This hospital had had a series of patients with post-operative ileus when the post-operative course should have been uneventful. Whereas the same surgeon working at St. Bartholomew's Hospital had not had a single case of ileus using a somewhat similar technique. The only difference being that at Bart's they gave 15 mg. of tubocurarine as opposed to 10 mg. and that they never gave prostigmine as they did not find it necessary. When they stopped giving the dose of prostigmine the result was dramatic, for they never had another case of ileus. As a matter of interest he had taken one hundred consecutive cases in which tubocurarine had been used and had found only one case of post-operative ileus, and this was in a patient who had well-developed general peritonitis at operation. In 50 cases in which gas-oxygen-trilene had been used for the covering anaesthesia there were double the number of pulmonary complications that occurred when cyclopropane had been used in a further 50 cases. This was not a climatic effect because the series ran concurrently. All the cases were abdominal sections.

In perineo-abdominal excision of the rectum he felt that spinal anaesthesia still held its position as there was distinctly more bleeding from the perineal end of the operation when curare was used. Admittedly blood replacement was comparatively easy, but he felt that the patient's own blood was better than the bottled variety. Dr. Gray had brought out a most interesting point about curare in that it could cause retention of urine and difficulty of micturition post-operatively.

Dr. William W. Mushin said that there is one marked disadvantage attached to the use of tubocurarine, namely, the serious bleeding that occurs at the site of operation. This had been a constant observation of his and had been confirmed by numerous colleagues up and down the country, both anaesthetic and surgical. The bleeding was probably due to the action of curare on the synapses in the sympathetic ganglia, and hyperventilation had no effect in lessening it. He gave two illustrative cases. For a long time he made a practice of infiltrating the abdominal wall with adrenaline in saline to obviate the tedium of the surgeon in tying innumerable vessels before getting on with the operation. At a meeting of this Section when anaesthesia for abdomino-perineal resection of the rectum was discussed, it was held by many present that curare was contra-indicated for this operation on account of the profuse haemorrhage during the perineal part of the operation (*Proc. R. Soc. Med.*, 1947, 40, 263).

An impression current among many junior colleagues was that spinal anaesthesia was outmoded. He was of the opinion that spinal anaesthesia still had a place in anaesthetics, and should be considered whenever a bloodless field in operations of the abdomen and pelvis had special advantages. The removal of vascular tumours in the abdomen and pelvis, and the repair of difficult herniae were instances of such operations for which spinal anaesthesia would contend with curare when the choice of anaesthetic was considered.

Dr. J. Kennedy Harper said that having used d-tubocurarine in a wide variety of cases, he felt that it was the drug of choice when muscular relaxation was required. The statement that increased bleeding

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The percentage of chest complications which I have recorded in this series is lower by far than my own percentage before the introduction of tubocurarine and considerably lower than most of the reliable reports. Figures are of little value because so much depends upon the criterion of what is and what is not a pre-operative chest complication, on the standard of pre-operative supervision of patients, the season, the climate, and the type of operation.

It is, however, useful to examine the anæsthetic factors accepted as predisposing to pulmonary complications and see how they are affected by the anæsthetic under consideration. Among the most vital of these factors are post-operative depression of the respiration and the cough reflex, prolonged periods of narcosis and immobility with possible respiratory obstruction, and the possible aspiration of vomitus. It is true to say that 90% of our patients who have had d-tubocurarine chloride have their pharyngeal and cough reflexes fully restored at the close of the operation and the majority are co-operative and talking by the time they leave the theatre. The main contributory factors are thereby removed and I do not believe that it is possible to achieve this with certainty in major abdominal and thoracic surgery with any other method of general anæsthesia. The part played by the anæsthetic in causing pulmonary complications must be very materially reduced. I would like to stress once again, however, that if there is one thing worse than returning the patient to bed with a respiration depressed by an anæsthetic agent, it is returning him to bed with his respiration depressed by d-tubocurarine chloride. This will undoubtedly predispose to the incidence of post-operative atelectasis.

(4) *Retention of urine:* There seems to be an increased incidence of post-operative retention of urine. There is, of course, quite a considerable incidence of post-operative retention after any anæsthesia even in those cases in which the operation could have contributed little towards its occurrence. Women are particularly prone to this complication, nervous patients and elderly men with incipient prostatism are also liable to develop it. A series of 127 abdominal cases were reviewed in an attempt to see whether there were any grounds for the complaints. This series did not include those gynæcological or genito-urinary procedures which might be predisposed to urological disturbance. Retention of urine occurred in 24% of these patients and just on 9% recovered after one or more injection of carbachol and 7.9% had to be catheterized. Records of 185 patients were consulted and compared with 137 cases who had not had d-tubocurarine chloride. 15% of those who had been given d-tubocurarine chloride had to have carbachol against only 9% of those who had not had tubocurarine. I think this is a difficulty and I have seen a case following lobectomy in a young male where the patient did not micturate naturally for seven days.

(5) *Difficulty in accommodation:* Lastly there is a tendency to difficulty in accommodation following operation. Four of my cases have complained that they were unable to read a newspaper for forty-eight hours. But I would ask with what other anæsthetic are they likely to try to read a paper so soon after major surgery?

What then is to be our verdict with regard to this substance? I believe that d-tubocurarine chloride is not the final answer, but the absolute certainty of results, its comparative non-toxicity and the ease of the anæsthesia in which it is used are factors which persuade me that, although we have not reached our ultimate goal we have indeed taken a most significant step. Griffith of Montreal observed the softening of electric convulsions by tubocurarine and in a flash of inspired genius saw its application to anæsthesia. He revolutionized our specialty by removing for all time the need for deep anæsthesia.

Section of Orthopædics

President—GEORGE PERKINS, M.C., F.R.C.S.

[December 2, 1947, concluded]

Leadbetter's Osteotomy.—F. P. FITZGERALD, F.R.C.S.

The treatment of non-union in fractures of the neck of the femur presents an incompletely solved problem. In an attempt to deal with it, Leadbetter devised an interesting operation (*J. Bone Jt. Surg.*, 1944, 26, 713).

Leadbetter's osteotomy.—This consists of a vertical osteotomy of the femoral neck. The details of the operation are as follows:

An anterior approach is made and the junction of the upper third with the lower two-thirds of the neck is defined. The outer fragment of the bone is then divided inwards as far as the fracture line. The new lower fragment is displaced medially and with force so that it rotates the head of the femur and comes to lie underneath it.

When this operation was described four years ago, the originator had treated 8 cases, and he had assessed them one year after operation. 6 were united by bone; 2 results were favourable. The author has treated 6 cases, using a modification of this method. Owing to wartime difficulties, 3 cases have not been located, and one is too recent to be able to assess the result. The remaining two fractures have got bony union and useful hips.

Modified osteotomy.—(1) It has been found easier to carry out the operation through a lateral approach, using X-ray control. (2) Leadbetter points out that it is important to cut the bone at the high level, and this is said to preserve the blood supply. This makes it difficult to rotate the head of the femur, and hence the bone has been cut at a lower level—at the junction of the lower third with the upper two-



FIG. 1.—An osteotome defines the line of bone section.



FIG. 2.—The lower fragment has been pushed medially and the head rotated. The greater trochanter has been displaced laterally.

thirds. No ill-effects have been noticed in this very small series of cases. The following case, which was demonstrated, illustrated these points.

A man, aged 50, was operated upon for an ununited fracture of the left femoral neck, using this modified osteotomy. Fig. 1 shows the fracture reduced, and the line of the bone section. Fig. 2 illustrates the end-result. Seven months from the time of operation, he was back at his full work without experiencing any pain. He is a packer, which entails standing for seven hours a day. His hip-joint is stable, and the joint movements are excellent, with the exception of rotation, which is absent. He has got just over half an inch of shortening.

followed its use needed qualification. Increase of bleeding could occur if the respiratory exchange of the patient was inadequate, thus producing an increase of carbon dioxide tension in the blood with an inevitable rise of blood-pressure. It was the anaesthetist's duty to prevent this by adequate aided respiration.

He had not seen bronchospasm in adequately anaesthetized patients. He had, however, seen the relief of bronchospasm in a chronic asthmatic patient who was given a curarizing dose of d-tubocurarine together with pentothal nitrous oxide-oxygen anaesthesia for a partial gastrectomy.

Dr. H. W. Loftus Dale was in entire agreement with Dr. Cecil Gray on his conception of the altered physiology relating to anaesthesia in the curarized patient.

It was impossible to overstress the importance of assisting inspiration to ensure against sub-oxygenation.

Dr. Gray had rightly emphasized the increased risk of "spill-over" of stomach content during gastric surgery to avoid which he intubated his patients. Dr. Loftus Dale had employed continuous gastric suction in all cases as an alternative method and had found it to be very satisfactory, having had a series of 47 partial gastrectomies with no post-operative pulmonary complications.

There was more bleeding than associated with spinal anaesthesia in the production of which capillary dilatation, diminished support to the venous system and an intact vasomotor system played a part. There was, however, another factor, the synergistic depressant action of thiopentone, cyclopropane and morphia on the respiratory centre leading to an increased tension of CO_2 , the response to which was masked by parietic muscles of respiration in the curarized patient.

Since morphia had been omitted there had been marked diminution in capillary oozing and the early rise in systolic blood-pressure reported by several observers.

For premedication he now used 100 mg. of pethidine and 1/150 grain (0.43 mg.) of hyoscine which produced adequate drying up of secretions and reasonable sedation.

No patient should be sent back to the ward curarized; if powerful poisons were used they should be eliminated before the patient left the hands of the anaesthetist. Finally the temptation to give that last 5 or 10 mg. at the end of the operation to assist closure of the peritoneum should be avoided; it was this Parthian shot which had done much to bring discredit to this most valuable aid to anaesthesia.

Dr. Donald V. Bateman drew attention to Dr. Gray's reference to the use of a face-mask and uncuffed endotracheal tube and also his mention of kemithal. He asked if Dr. Gray had some special reason for not using a cuffed tube to eliminate the hazard of inspired gastric contents and if he had the impression that kemithal was preferable to thiopentone for maintenance of a curarized patient.

Dr. Cyril Scurr mentioned a case which illustrated the value of a test dose of d-tubocurarine chloride.

The patient, a woman aged 56 and weighing 10½ stones, gave the history that a year previously she had suffered from ptosis affecting the left eye when she was tired; after three months' treatment with prostigmine this symptom cleared up. At the time of operation she was free from myasthenic symptoms and had not had any treatment for nine months.

She was given a test dose of 4 mg. of d-tubocurarine chloride intravenously; two minutes afterwards she was completely paralysed, being unable to open her eyes or move her limbs, the tidal air was much reduced. She was then given 0.25 gramme of soluble thiopentone and light general anaesthesia was maintained with cyclopropane, the respiration being assisted.

Profound muscular relaxation persisted throughout the operation for total hysterectomy, which lasted fifty minutes. At the end of operation the tidal air was adequate.

At no time were this patient's myasthenic symptoms more than minimal and in a less observant subject they might well have gone unnoticed; in the absence of information provided by the test dose, a grave overdose of d-tubocurarine might have been given.

Dr. T. C. Gray, in reply, thanked Dr. Frankis Evans for his interesting and helpful remarks. He had always considered it important to prevent the undesirable parasympathomimetic effects of prostigmine used as an antidote to tubocurarine by administering with it an adequate dose of atropine. It seemed quite possible that the administration of unbuffered prostigmine might result in depression of the intestinal movements after the initial stimulation.

In his experience this technique had proved entirely satisfactory for œsophagoscopy but less so for bronchoscopy because of the occasional occurrence of respiratory spasm. In a busy centre, however, when there were many bronchoscopies to perform in a limited time, the method was considerably less time-consuming and more pleasant for the patient than local analgesia.

He was sorry to have misled Dr. Bateman for he frequently employed a cuffed tube for upper abdominal and chest surgery, in fact whenever there was a danger of regurgitation. He agreed with Dr. Bateman that this was the safest and most satisfactory method.

Section of Orthopædics

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applied by a slightly modified Fiske's method, which allowed a total range of assisted active movement of about 90 degrees at hip and knee joints while the traction continued to act. A weight of 5 lb. was employed for the first three days, and was then gradually increased to 20 lb. by the twelfth day and retained there until three months after the operation. Faradism and static exercises to the quadriceps were started immediately, and graduated assisted active movements of the new joint (with the traction still acting) from the tenth day.

Three months after operation the traction was removed; assisted active exercises continued, but a straight back-splint had to be provided for night use on account of persistent slight limitation of active extension due to the quadriceps slack. Two weeks later the patient started walking with a hinged knee-cage, and at that time her range of movement was about 85 degrees as shown in the X-ray (fig. 1A and B).

She now has full extension and 90 degrees of flexion movement, with so little slack in the quadriceps that the back-splint has been given up. The knee is painless, cool, and free of swelling, the movement is smooth, and there remains only quite moderate lateral instability though it is felt to be safest to continue the use of the hinged knee-cage. Function is greatly improved.

This case supports Mr. Stamm's contention that a perfectly satisfactory arthroplasty can be produced without the use of metal, or of soft-tissue flaps interposed between the bone ends, provided that correct after-treatment is given, the essential points in this being: (a) Continuous traction for about three months in the case of major joints, increasing gradually from an early minimum to the maximum in about two weeks, and (b) daily assisted active movements starting in about ten days, and being performed with the traction acting all the time. In the knee-joint, I believe that removal of the posterior projecting portions of the femoral condyles is also essential.

II.—Caries of Spine: for Diagnosis.

R. W., male, aged 25.

29.12.47: Developed a pyrexial illness with dorsilumbar pain.

1.1.48: General practitioner found a localized area of tender spasm in sacrospinalis. Local injection here of procaine produced temporary relief of pain.

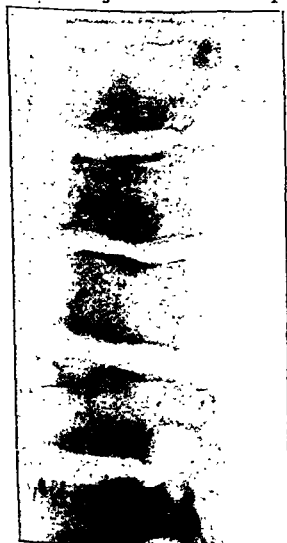


FIG. 2.—Case II.

7.1.48: A subcutaneous swelling appeared, in and to both sides of the mid-line, overlying and obscuring the upper lumbar spinous processes. Swinging pyrexia continued. Admitted to local hospital. Penicillin 250,000 units intramuscularly b.i.d. prescribed.

9.1.48: X-ray (fig. 2): An area of erosion in the upper and anterior part of the body of the second lumbar vertebra, with moderate marginal sclerosis and some lipping at the anterior angle. Very little disc narrowing. Blood-count: moderate polymorph leucocytosis. Aspiration of swelling: 2 oz. of thick yellow pus. Penicillin 250,000 units injected into the abscess. Cultures produced a pure growth of *Staphylococcus aureus*, penicillin-sensitive, coagulase-positive.

13.1.48: Temperature normal. Abscess had refilled. Re-aspiration of abscess: 2 oz. of thinner pus containing the same organism on culture. Penicillin 250,000 units injected into the abscess.

17.1.48: Remained apyrexial. Penicillin stopped.

16.2.48: Transferred to County Hospital, Pembury.

Symptom-free at rest. Moderate stiffness of back. Slight upper lumbar kyphosis. No sign of abscess. Lasègue's sign 80 degrees in each leg. Doubtful left extensor plantar response and doubtful bilateral ankle

[March 2, 1948]

Four Cases shown by J. H. MAYER, F.R.C.S.

I.—Arthroplasty of Knee.

Mrs. E. W., aged 55.

History.—Rheumatoid arthritis affecting hands and wrists for many years, knees since 1942 and shoulders since 1945.

The left knee had been arthrodesed in 1945, at which time the right knee functioned quite well, but since then the right knee has become worse fairly rapidly. When seen in June 1947 the joint was slightly warm, with moderate synovial thickening and slight tenderness; extension was limited by 10 degrees, and a range of less than 30 degrees of flexion was allowed from this point accompanied by considerable pain. There was great difficulty in walking, and greater in climbing stairs and in getting into and out of a chair, due to the bilateral stiff knees. E.S.R. was 26 mm. in one hour. X-rays showed gross narrowing of the joint space with marginal new bone formation. The left knee was ankylosed by bone in good position.

Operation.—Arthroplasty of the right knee was performed on 30.7.47. It was decided to try this operation despite the appearances of subacute activity in this joint because its muscles were better than those on the left, and because arthroplasty could be performed later on the left if it failed on the right, whereas if it succeeded on the right a second operation would be avoided.

Through an anterior horse-shoe incision the patella was excised and a complete synovectomy performed. All remains of articular cartilage were removed from femur and tibia, and the posterior projections of the femoral condyles were removed completely, thus leaving a convex surface of far smaller diameter than before, round



FIG. 1A—Case I.



FIG. 1B—Case I.

which the slightly hollowed tibial condyles should glide. A median antero-posterior crest was left on the tibia to articulate in the intercondylar notch of the femur in an attempt to increase the stability of the new joint. The internal and external lateral ligaments of the joint were left intact so far as possible. The incision was closed in two layers, leaving the bare cancellous surfaces of femur and tibia apposed without the intervention of tissue-flaps or other structures. An error was made in not shortening the patellar tendon, and this led to some residual slack in the quadriceps for a considerable time.

After-treatment.—From a Steinmann pin through the tibial tuberosity, traction was

but fortunately far enough back to have missed the tibial articular cartilage; it should have been inserted $\frac{1}{2}$ in. higher and have been directed rather more forwards.

After-treatment.—Apart from soft dressings, the joint was not immobilized. Immediate active exercises were prescribed, and after removal of the sutures on the twelfth day all joints regained their ranges of movement rapidly. Normally I should have applied a walking plaster boot four to six weeks after operation until removal of the screws, but in this instance the patient, a medical colleague, was allowed to go home on crutches without plaster as I could rely on his obeying instructions not to put the foot to the ground, and because he wished to leave hospital early for other reasons.

On 13.8.47, ten weeks after the first operation, the screws were removed. Active exercises were maintained, and walking was resumed two weeks after this second operation.

The patient, who is a keen sportsman, made a rapid recovery, and resumed work in general practice within a few weeks. The only abnormal physical sign now, apart from the operation scars, is a trace of limitation of plantar-flexion of the foot. He plays vigorous squash, tennis, &c., without symptoms.

I believe that all major ankle fractures with displacement of the posterior malleolus or diastasis of the inferior tibio-fibular joint should be treated by open reduction and screwing. It is practically impossible to secure perfect reduction by any other means, and screwing also allows early post-operative mobilization to ensure a good functional result. The screws should be removed after about ten weeks in view of their proximity to the joint.

IV.—Infective Arthritis of Hip-joint : Plaster Bed with Traction.

J. G., male, aged 26.

History.—Aching pain in right hip, followed later by a limp, starting in July 1947. No relevant previous history or family history.

On admission (29.11.47).—Apyrexial. Right buttock wasted. Gross limitation of all movements of right hip-joint, with pain on forcing in any direction but painless at rest. No sign of effusion or abscess.

X-ray (fig. 5): Right hip shows narrowing of joint space, with mottling of head and neck of femur and apparent sequestration of a fairly large segment of the upper part of the femoral head.

Blood-count normal. E.S.R. 4 mm. in one hour. Mantoux positive at 1 : 400, negative at all greater dilutions.

Diagnosis.—Low-grade non-specific infective arthritis of the hip-joint.

Treatment.—The patient has been immobilized in a plaster bed with traction on the affected limb. This type of plaster bed has been in use at the County Hospital, Pembury, for several years, and was developed there during the late war by Messrs. W. W. Gilford and R. H. Bolton.

The plaster bed is mounted on a metal stretcher (an ordinary E.M.S. stretcher with the wire mattress removed) by two transverse metal or wooden rods fixed to the undersurface of the bed by plaster and resting on the side-bars of the stretcher (fig. 6). One additional similar support under the head-piece of the bed rests on the upper transverse bar of the stretcher. These mountings merely rest on the stretcher, so that the whole bed can be lifted from the stretcher for turning.

This method of mounting is economical in scarce materials such as timber, and it greatly facilitates nursing. For ordinary nursing the stretcher rested on a normal bed-frame leaves space for bed-pans to be placed under the patient without lifting. Stretcher, bed and patient can be lifted easily by two to four people on to a stretcher-trolley, X-ray table, operating table, &c. Alternatively the patient can be nursed

clonus, but these were not confirmed at re-examination. X-ray appearances unchanged. Blood-count normal. Mantoux weakly positive at 1 : 10,000. Recent scar of a large boil in right scapular region, which had ruptured and discharged slowly three months before onset of present illness. No other relevant previous or family history.

Treated by very gentle mobilization, the patient remains symptom-free and lumbar mobility has increased. Lumbar kyphosis remains unchanged.

This case appears to have a double pathology: (a) Old vertebral epiphysitis previously undiagnosed, and (b) subcutaneous abscess of the back arising by hæmatogenous or lymphatic spread from the recent boil over right scapula.

The sclerosis and new-bone formation seen in the X-rays ten days after the onset of symptoms are not consistent with a diagnosis of staphylococcal osteomyelitis of the vertebra.

POSTSCRIPT.—When last seen in June, 1948 he remained symptom-free. Physical signs and radiological appearances remained unchanged apart from rather freer mobility of the spine, and there were no abnormal signs in the central nervous system.—J. H. M.

III.—Pott's Fracture treated by Internal Fixation.

K. J., male, aged 24.

The patient sustained the fracture shown in fig. 3 on 3.6.47, consisting of fractured medial and posterior malleoli of the tibia, fractured lower shaft of the fibula, posterior subluxation of the ankle-joint and slight diastasis of the inferior tibio-fibular joint. Two attempts at closed reduction elsewhere had failed to achieve good position.

Operation.—On 4.6.47 I performed open reduction and screwed the fragments back into place. The patient was placed in the prone position with his foot over the end of the table. The posterior malleolus was dealt with first, through a postero-medial incision with inward retraction of the flexor structures and stripping of the

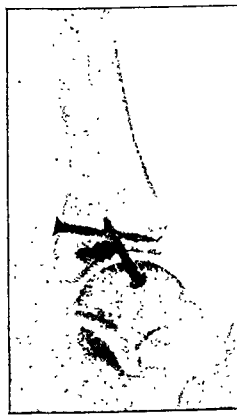


FIG. 3A.—Case III.

FIG. 3B.—Case III.

FIG. 4A.—Case III.

FIG. 4B.—Case III.

lowest fibres of flexor hallucis longus from the fibula. This fragment is always very difficult to reduce and to retain in position, and the following method was used: A Steinmann pin was inserted into the fragment from behind and used as a lever to pull it down into position; once this had been achieved the pin was quickly driven into the tibial shaft to maintain the reduction while drilling and screwing were performed, and the pin was then removed. A long screw was then inserted across the inferior tibio-fibular joint, and finally the medial malleolus was screwed into position. The post-operative X-ray (fig. 4) shows that the second screw lies dangerously low,

Section of Psychiatry

President—Professor Sir DAVID K. HENDERSON, M.D., F.R.C.P., F.R.S.E.

[May 11, 1948]

The Technique and Application of Electronarcosis

By A. SPENCER PATERSON, M.D. and W. LIDDELL MILLIGAN, M.D.

Dr. A. Spencer Paterson:

About two years ago the situation with regard to electroshock therapy was not altogether satisfactory. In different hospitals, there were being passed through patients' brains electric currents which differed from each other in every particular and there was little experimental work to show which were safe and which were dangerous. The ill-effects produced by the most unsatisfactory types of current were considered by some psychiatrists to be sufficient grounds for employing the treatment as little as possible, if indeed they did not condemn it altogether.

Again, there were many psychiatric conditions which failed to improve when the patient was given only two or three convulsions per week. It had, however, already been demonstrated, especially at Portsmouth, that the more intense administration of electroshock could effect a recovery in otherwise intractable cases. Although the immediate and later side-effects of these heroic methods were not serious, nevertheless careful nursing was often necessary.

One was thus anxious to discover some method which would combine as good or better a therapeutic result with little discomfort or danger to the patient.

We therefore were interested to find that van Harreveld (1934), working first in Holland and later at Los Angeles in California, had been studying the effect of passing a relatively low current through the brains of animals for a period of several minutes, a procedure which he called "electronarcosis". With the distinguished pathologist, Globus (1943), he showed that in dogs currents three or four times as strong as those used initially in electronarcosis in man and lasting many times as long (even up to seventy-five minutes) produced no histological changes that could be discovered post mortem. Dr. E. B. Tietz (1947), working in a neighbouring mental hospital, and other psychiatrists reported favourable results with this method in the treatment of schizophrenia.

COMPARISON OF ELECTROSHOCK, ELECTRONARCOSIS AND CONTROLLED ELECTROSHOCK

In electroshock a relatively high current is passed through the patient's brain for a fraction of a second. The current varies with the type of machine used. Some of these allow a current of 1,200 to 1,500 ma. to pass during a fraction of a second and it is even stated of one machine on the market that "it is impossible for a current of more than 2,000 ma. to pass through the patient's brain" (fig. 1). In our electroshock machine (Paterson, 1946), however, an alternating sinusoidal current of about 250 ma. is passed for about half a second.

The typical course of events in an electrically induced convulsion is as follows: There is a sudden momentary contraction usually of the extensor muscles of the spine, often with flexion at the hips and elbows. Then there is a latent period of about seven or more seconds, when the muscles relax either partially or completely. This is followed by extreme opisthotonus and a tonic phase for about ten seconds, after which violent clonic movements occur until the forty-fifth second or later when respiration becomes re-established. The heart may be inhibited for two or three seconds at the onset.

Electronarcosis on the other hand begins with a modified convulsion. The chief points of

permanently on a trolley instead of a bed, and is in this way correspondingly more mobile when being nursed out of doors or at home, and when attending occupational therapy and other departments in the hospital.

Traction on the affected limb is applied through extension strapping applied to calf or thigh and calf. The leg-gutter of the plaster bed is prolonged distally on the affected side and has no foot support. The traction cord passes in the line of the limb from a spreader below the heel to a horizontally-mounted pulley fixed on wood at the distal end of the leg-gutter; traction at any desired tension is maintained by a spiral spring linking the cord beyond the pulley to the plaster-bed mounting (fig. 7).



FIG. 5.—Case IV.



FIG. 6.—Case IV.



FIG. 7.—Case IV.

Counter-traction is effected by friction between patient and plaster, and by the sole of the opposite foot pressing against its foot-rest. Drop-foot on the affected side is prevented by a removable arch of Kramer wire supporting a mobile foot-rest and preventing bedclothes pressure. This method allows traction with complete immobilization in optimum position for the affected joint (hip or knee), and is equally useful in adults or children.

I am extremely grateful to Messrs. Gilford and Bolton for permission to demonstrate and publish this case before the appearance of their own paper on this type of plaster bed. The credit for its invention belongs entirely to them.

Section of Psychiatry

President—Professor Sir DAVID K. HENDERSON, M.D., F.R.C.P., F.R.S.E.

[May 11, 1948]

The Technique and Application of Electronarcosis

By A. SPENCER PATERSON, M.D. and W. LIDDELL MILLIGAN, M.D.

Dr. A. Spencer Paterson:

About two years ago the situation with regard to electroshock therapy was not altogether satisfactory. In different hospitals, there were being passed through patients' brains electric currents which differed from each other in every particular and there was little experimental work to show which were safe and which were dangerous. The ill-effects produced by the most unsatisfactory types of current were considered by some psychiatrists to be sufficient grounds for employing the treatment as little as possible, if indeed they did not condemn it altogether.

Again, there were many psychiatric conditions which failed to improve when the patient was given only two or three convulsions per week. It had, however, already been demonstrated, especially at Portsmouth, that the more intense administration of electroshock could effect a recovery in otherwise intractable cases. Although the immediate and later side-effects of these heroic methods were not serious, nevertheless careful nursing was often necessary.

One was thus anxious to discover some method which would combine as good or better a therapeutic result with little discomfort or danger to the patient.

We therefore were interested to find that van Harreveld (1934), working first in Holland and later at Los Angeles in California, had been studying the effect of passing a relatively low current through the brains of animals for a period of several minutes, a procedure which he called "electronarcosis". With the distinguished pathologist, Globus (1943), he showed that in dogs currents three or four times as strong as those used initially in electronarcosis in man and lasting many times as long (even up to seventy-five minutes) produced no histological changes that could be discovered post mortem. Dr. E. B. Tietz (1947), working in a neighbouring mental hospital, and other psychiatrists reported favourable results with this method in the treatment of schizophrenia.

COMPARISON OF ELECTROSHOCK, ELECTRONARCOSIS AND CONTROLLED ELECTROSHOCK

In electroshock a relatively high current is passed through the patient's brain for a fraction of a second. The current varies with the type of machine used. Some of these allow a current of 1,200 to 1,500 ma. to pass during a fraction of a second and it is even stated of one machine on the market that "it is impossible for a current of more than 2,000 ma. to pass through the patient's brain" (fig. 1). In our electroshock machine (Paterson, 1946), however, an alternating sinusoidal current of about 250 ma. is passed for about half a second.

The typical course of events in an electrically induced convulsion is as follows: There is a sudden momentary contraction usually of the extensor muscles of the spine, often with flexion at the hips and elbows. Then there is a latent period of about seven or more seconds, when the muscles relax either partially or completely. This is followed by extreme opisthotonus and a tonic phase for about ten seconds, after which violent clonic movements occur until the forty-fifth second or later when respiration becomes re-established. The heart may be inhibited for two or three seconds at the onset.

Electronarcosis on the other hand begins with a modified convulsion. The chief points of

difference are as follows: The electroanæsthesia machine (Paterson and Milligan, 1947) has an electromagnetic device which automatically keeps the current constant and it can be regulated by means of a rotary stud. Instead of giving a sudden violent stimulus to the patient's brain from a relatively high current, one gradually raises the current from zero to 200 ma. in the course of about two seconds. This current passes for thirty seconds and is slowly reduced over a period of fifteen seconds to about 70 ma. or lower until the patient starts to breathe. The initial cardiac inhibition is generally of no greater duration than in electroshock. The patient starts to breathe again at the same time as he would have done

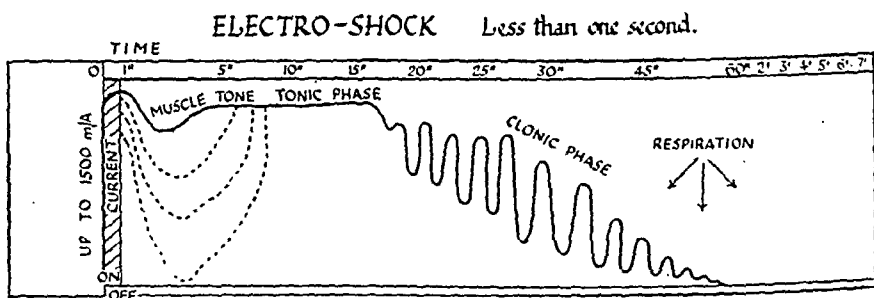


FIG. 1.

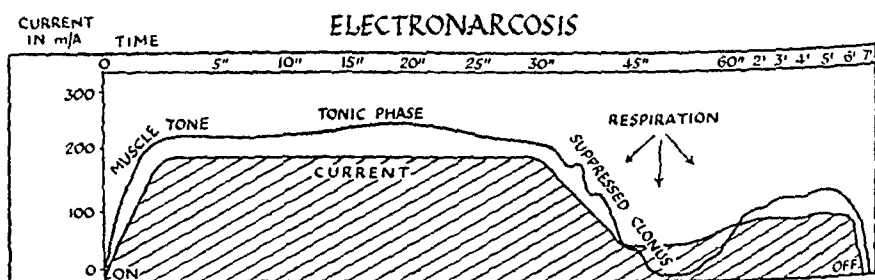


FIG. 2.

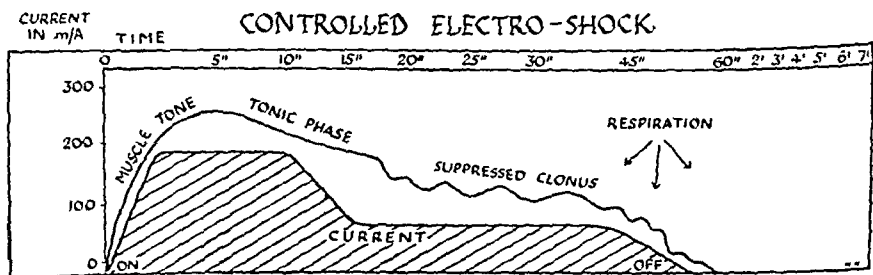


FIG. 3.

Comparison of electroshock, electronarcosis and controlled electroshock. Charts showing muscular reaction to current variations in relation to time (after Tietz, Olsen and Rosanoff).

after electroshock. The gradual increase or decrease of the current reduces side-effects such as headache and temporary disturbances of memory. The clonic movements begin at thirty seconds when the current is reduced. The patient's clonic movements are less violent because both agonists and antagonists are still in a state of increased tonus. The avoidance of violent clonic movements prevents fractures or injuries. The current is then slowly raised until there is flexion at the elbows and a slight degree of respiratory stridor. Further slight increases of current are continued until the end of treatment at about seven minutes (fig. 2).

The term "controlled electroshock" is given to the procedure of raising the current to 200 ma. in two seconds for seven to twenty seconds and gradually reducing it until respiration is again re-established (fig. 3).

The treatment is given three or four times a week for twelve times. After a rest of some days another course of six or twelve treatments may be given. Dr. Glyn Davies and I have given over 750 treatments.

TECHNIQUE OF ELECTRONARCOSIS

First of all in the history we ask particularly regarding diseases of the heart, lungs and vertebral column, just as we do before giving electroshock. If a patient is sufficiently robust to tolerate electroshock, it is likely that he will be sufficiently strong for electronarcosis, especially if a quick-acting barbiturate and curare are given. Where curare is given, one must include in the oxygen apparatus a bag of india-rubber which can be deflated into the patient's nose and mouth in a rhythmic manner, if respiration should ever become insufficient. One should have at hand cardiac stimulants and adrenaline, and, where curare is used, an ampoule of prostigmine, which is its antidote.

We always take an electrocardiogram before treatment.

It is better to give a quick-acting barbiturate beforehand, either 3 grains of seconal by mouth, or better 0.3 - 0.5 gramme of pentothal or sodium amytal intravenously. Sodium amytal has the advantage of keeping the blood-pressure lower and also if, as occasionally happens, the patient suffers unduly from headache or malaise, it allows him to sleep until those symptoms have disappeared so that he wakes up in a comfortable state. Its disadvantage is that it takes more time to take effect compared with pentothal. Barbiturates make it less likely that there will be any unpleasant reflex phenomena like apnoea or temporarily feeble action of the heart. One-sixtieth of a grain of atropine is also given, preferably i.v. Atropine inhibits excessive salivation, and also prevents cardiac and respiratory inhibition from overaction of the vagus nerve. We generally give curare in doses of about 2 mg. per stone of body-weight. With new patients we start with a small dose before pentothal to make sure that there is no idiosyncrasy. Ordinarily it is given after pentothal through the same needle from a different syringe. Treatment is started three minutes afterwards. Curare prevents compression of vertebrae, eases the strain on the heart and enables one to feel the pulse more readily. It does not appear to keep the blood-pressure lower.

A medium-sized pessary makes the best gag. An airway is sometimes necessary.

COMPLICATIONS ENCOUNTERED IN TREATMENT

Saliva or mucus may collect in the larynx or trachea unless prevented, as stated, by atropine. Sometimes one has to wipe ropy mucus out of the throat with a swab several times. Burns cannot occur if the electrodes are flat and make contact with the forehead by means of lint soaked in a saturated solution of salt.

Sometimes the patient complains later that he has become conscious during the treatment. He may say that he could not speak but only make movements of the arms to indicate that we must turn off the current. The experience may be very frightening because the patient may feel suffocated and also see bright flashes of light or hear loud noises. This complication is more likely to happen to older patients who require a higher current. Except in small patients or young patients with brisk knee reflexes, we seldom give less than 200 ma. for the first half-minute. If the patient begins to have clonic movements before the end of the first half-minute (that is, when the strong current is still passing), then he is more likely to become partially conscious later unless care is taken. One must regulate the dose according to the physical signs, since the necessary dose varies from patient to patient. Strong flexion at the elbows and a slight stridor show that the correct level is reached. Sometimes it is necessary before the end of treatment to put the current up to as high as even 170 ma. especially if the patient has had barbiturate.

It is necessary to examine the blood-pressure several times during treatment, especially in older patients, because a pressure which has been normal at first may rise in older subjects to as high as 260/160. If the diastolic pressure rises above 130 mm., it is better to switch off the current. The rate and volume of the pulse should also be observed. A poor volume often becomes satisfactory by lowering the current merely 5 ma. We believe that cardiac inhibition is more apt to occur in young subjects, especially those with brisk reflexes. In these cases intravenous pentothal and atropine are necessary and the current should be temporarily lowered and in severe cases cut, if there are signs of respiratory or cardiac embarrassment. We have not had any anxiety in this type of case. If in the later minutes the pulse were suddenly to become very rapid and feeble, or if there were irregularity of the pulse other than occasional extrasystoles, or if there were any signs of respiratory distress, then one should switch off at once.

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ELECTRO-SHOCK Less than one second.

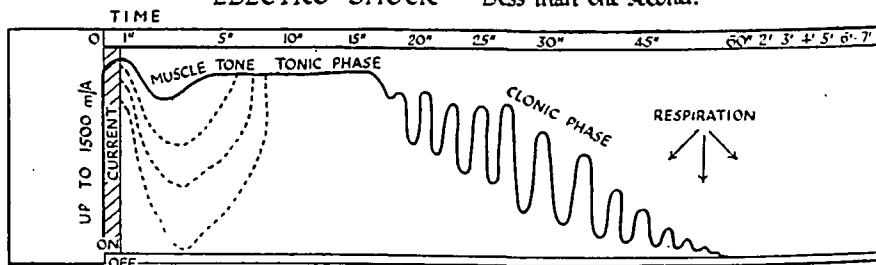


FIG. 1.

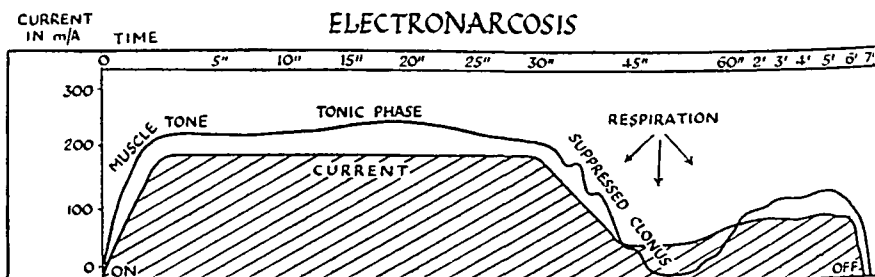


FIG. 2.

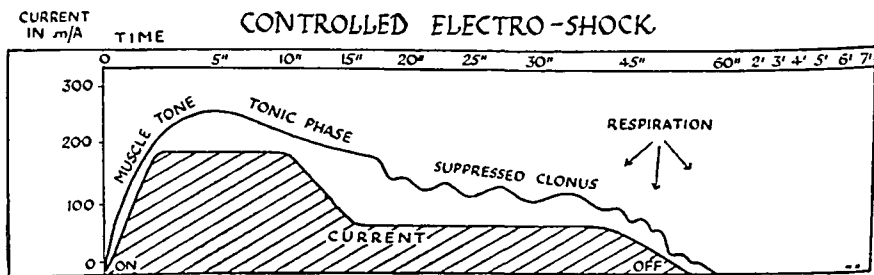


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TABLE II.—ELECTROSHOCK AND ELECTRONARCOSIS COMPARED IN SCHIZOPHRENIA

Of 14 cases which failed with electroshock

6 recovered with electronarcosis. 3 made greater improvement. 5 no better.

shock had helped the electronarcosis to take effect, as there is, no doubt, a synergic action between the two.

It is perhaps worthy of comment that Medlicott (1947) has found that there is a greater degree of lymphocytosis after electronarcosis than after electroshock, and also that the blood-sugar curve is both higher and of longer duration.

We may also remark here that electronarcosis is in one respect safer than insulin coma therapy, for if in electronarcosis the patient appears to have undue cardiac or respiratory distress, then we can easily switch off the current, but if the patient's condition under insulin coma gives rise to anxiety, then the administration of intravenous glucose may take time and cause some difficulty.

STATES OF SEVERE DEPRESSION

Up till three months ago we had treated 16 cases of severe depression with electronarcosis, of whom 13 had already failed with electroshock. Of these 16 cases, 12 made a good recovery. The remaining 4 did not show any lasting improvement (Table III).

TABLE III.—SEVERE MELANCHOLIA TREATED WITH ELECTRONARCOSIS

Total	Recovered	Failed
16	12	4

The following are cases in this group:

Mrs. B., aged 41, had been depressed for one year. She had had marital difficulties, as her husband was 23 years older than she. She had tried to solve her problem by becoming an energetic business woman. The onset of her illness coincided with business worries. She had been actively suicidal prior to admission. After 8 treatments with electroshock she was still actively suicidal and desperate, but after one treatment with electronarcosis she stated that this was something quite different, and she later attributed her complete recovery to the course of electronarcosis which she received.

Miss C., aged 57, had for one year gradually developed a condition of severe agitated melancholia. She said that the Devil had made her conscious of sexual desires that were driving her insane. A full course of electroshock in another hospital had caused only temporary improvement, but after 9 electronarcosis treatments she made a perfect recovery.

In cases of chronic depression where electroshock has failed, it has been usual for the psychiatrist to consider having a leucotomy performed. Since, however, it has been found that electronarcosis frequently effects a recovery after electroshock has failed, we may expect that still more patients will not be submitted to this operation.

ELECTRONARCOSIS IN THE PSYCHONEUROSES

We have treated 9 cases of severe psychoneurosis with electronarcosis. Only one of these failed to improve. Two of the most striking recoveries were in states of panic.

Mr. D., aged 42, had been a widower for nine years. He had been head of a large factory during the war and had worked often for sixteen hours a day. He had developed a duodenal ulcer seven years before and had had a severe hæmatemesis. He returned to work too soon, and later became subject to severe claustrophobia.

For two years before being seen he had suffered from attacks of panic. In the street he would cling to the railings, stagger into a telephone box and call for a taxi to take him home. His firm had been very anxious to have him back but he had not worked during these two years. Psychotherapy alone had failed to make any difference. He had a second hæmorrhage during this period.

He was given 8 treatments with electronarcosis. His physical and mental state underwent a remarkable change for the better. He could go anywhere without fear and within two months was back at work looking and feeling well, and writing a scientific monograph. He had put on 7 lb. in weight.

Mrs. E. was a young woman with two children. During the war she had suffered agonies of anxiety over her husband who was in great danger in the front line. After the birth of her second child she had developed ideas that there might be a skeleton or a ghost that would open the door and terrify her. She had to leave her house. Her attacks of panic were distressing to witness and were quite impervious to psychotherapy. She made a complete recovery after 12 treatments with electronarcosis, without any ill effects.

Two other psychoneurotics were chronic hysterics with depressive affect who improved immediately so that psychotherapy had more effect. Two were very severe obsessives with depressive affect and both were very greatly improved. One was a man who had had about 50 examinations of his urinary passages in ten years and who had been impotent for eighteen months. He stated that he would commit suicide if he were not helped. He made a

If the patient is not given a barbiturate, he will probably wake up very quickly after the treatment. I have seen three patients in one day having breakfast and smiling happily within a quarter of an hour after treatment.

Dr. Tietz sends some ambulant patients home half an hour later, a procedure, however, that we would not recommend, but which is worth mentioning if only to counteract the impression that electronarcosis is unduly dangerous.

Occasionally the following symptoms occur temporarily after treatment—headache, lassitude, a sensation of constriction round the chest, amnesia, or difficulty of focusing. There may be some euphoria or confusion. Very often, however, the patient experiences no discomfort whatever.

Although, especially in schizophrenics who have recovered, there may be amnesia for the symptoms of the past illness, there is little or no amnesia for current events after the treatment is completed.

Although the technique may be thought to be rather complicated from what I have said, yet it is really quite easy to learn and one soon acquires confidence.

RESULTS OF TREATMENT

Schizophrenia

Up to three months ago we had 35 schizophrenics whom we had treated with electronarcosis. Some of these, however, had their treatment, or part of it, at Portsmouth and are included among Dr. Milligan's cases. Although his figures for schizophrenia will be more comprehensive, yet the accompanying tables are worth quoting because they bring out different points in the results.

It will be seen that these cases fall into three groups (Table I). First there are 9 cases who had previously had a schizophrenic episode from which they recovered. Of these 9,

TABLE I.—ELECTRONARCOSIS IN SCHIZOPHRENIA

	Total	Recovered and working	Improved and working	No, or slight, improvement
GROUP I				
Previous attack with recovery	9	7 at work	1 at work	1
GROUP II				
Ill less than 1 year . .	10	7 at work	2 at work	1
GROUP III				
Ill more than 1 year.				
Av. 3.2 years	16	4 at work	3 at work	9

8 were back at work in three months, while only one was not improved. The second group consisted of 10 patients who had been ill for less than twelve months since first seen and 9 of these returned to work. Two of these, however, still showed mild symptoms. The remaining case, though not recovered, had much improved. The third group consisted of 16 patients who had been ill for more than a year when first seen, the average duration of the illness being 3.2 years. Of these 16, 4 made a complete recovery. 3 more were able to return to work but still retained mild symptoms. The other 9 were greatly improved, in some cases from being violent and disturbed to being quiet and well behaved and regaining some insight.

Both Tietz (1947) in California and Medicott (1947) in New Zealand have reported that older paranoid types do better than the younger hebephrenic groups, and these older groups I believe do better with electronarcosis than with insulin. The following is a case of a paranoid involutional patient with catatonic symptoms who made a good recovery.

Mrs. A., aged 51, had been hypochondriacal for ten years, and then depressed for six months. She was actively suicidal and razor blades were found under her pillow. She heard voices saying that she would be arrested and executed. She had periods of cataleptic stupor alternating with wild catatonic excitement. She had already had a few electroshocks elsewhere with no success. After 18 treatments with electronarcosis, however, she returned home and has been carrying out all her household duties since then, in good health.

COMPARISON OF RESULTS OF ELECTROSHOCK AND ELECTRONARCOSIS

The effect of electronarcosis on cases of schizophrenia is comparable to that of an intensive course of electroshock. I believe, however, that electronarcosis produces better results while at the same time subjecting the patient to less physical strain. We treated 14 cases of schizophrenia after electroshock had failed and in 9 of these the response was more favourable with electronarcosis. In 5 cases there was no better response with electronarcosis than with electroshock (Table II). In 6 out of 14 cases where electroshock had failed, electronarcosis effected a recovery. In these cases, however, it is likely that the previous electro-

We are still unable to explain why patients look and feel so much better after a few treatments, or why chronic skin diseases should clear up. Cerletti, for instance, told me that he effected a recovery in 14 out of 16 cases of psoriasis by means of electroshock. His theory that the brain develops a specific substance when threatened with approaching death is still unproved. It may be, however, that these remarkable changes are effected in part by endocrine means, particularly through the pituitary.

CONCLUSION

With regard to electronarcosis and kindred treatments, I believe that we are only at the beginning. At the present time the following investigations are being carried out at the West London Hospital or elsewhere: Psychological tests before and after treatment; blood-pressure investigations, including that of the retinal artery, intra-arterial blood-pressure, blood and cerebrospinal fluid changes, and changes in the electro-encephalogram.

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Dr. W. Liddell Milligan: In dealing with the clinical applications of electronarcosis I intend to devote most of my remarks to its use in the treatment of schizophrenia. The case material has been provided by 120 patients treated at St. James Hospital, Portsmouth. Of that number there are 70 cases of schizophrenia, 15 of acute schizophreniform reaction or atypical schizophrenia, 10 cases of paraphrenia, 10 of melancholia and 15 of psychoneurosis, mostly anxiety states.

With regard to the schizophrenic groups the question of diagnosis immediately arises, but I have endeavoured to exclude the atypical cases which, although they exhibit evidence of schizophrenic reaction, were probably more allied to either manic-depressive or confusional states.

METHOD

As regards the method, I have nothing to add to the description already given except to confirm that if the technique is carried out properly the patient does not receive any unpleasant sensations. We have now given approximately 2,500 treatments and, except in the paraphrenic group, no patient has refused to continue treatment and there has certainly been no apprehension, indeed many impartial observers have commented upon the cheerful and composed manner of patients awaiting, let us say, their twentieth treatment. Especially in cases of schizophrenia, it is essential to give at least thirty treatments, before assuming that the therapy is not producing the desired response. In the present series, the average number of treatments per patient has been twenty.

RESULTS

When we come to results, I am giving the following without comment as it is of course much too early to draw any definite conclusions: of the 70 schizophrenics treated, complete remissions were produced in 44%, social recoveries in 17%, social defects in 8%, while 16% were improved in hospital and in 14% no improvement was obtained (Table I). This group includes 10 children under the age of 16 who had been sent to us from various parts of the country. I think that it would be better to omit these children when considering

remarkable improvement with only six treatments, becoming bright and happy and losing his obsessions. Lately, however, after six months there has been a slight return of symptoms. A woman who had had torticollis for seven years made a striking improvement for six months but she too has relapsed slightly. Another suffered from such severe torticollis that she was in constant pain. After electronarcosis the pain ceased and there was a progressive disappearance of the symptoms during the subsequent three months, so that now she is normal.

Tietz reports 9 recoveries out of 13 cases of chronic severe psychoneurotics.

RATIONALE OF ELECTRONARCOSIS

I should like to add a few words about the theoretical mode of action of electrocerebral treatment. Adolf Meyer's doctrine of reaction types has proved on the whole to be a valuable one. He speaks, for instance, of the catatonic, the manic, the melancholic, or the chronically anxious patient, as having reacted to environmental stress by adopting a special type of reaction. Meyer thought of this reaction type as being modifiable by treatment such as rest, or by withdrawing the patient to the quiet of hospital under a sympathetic and understanding physician who could influence him at the conscious level.

The remarkable and unexpected success, however, of these recent physiological treatments in the psychoses or intractable psychoneuroses suggests that we must visualize the morbid reaction type as depending on a particular reaction pattern or "set" at the autonomic level of the nervous system, for they act below the level of consciousness.

It has been found that such reaction patterns may be produced experimentally by certain drugs. Bulbocapnine, for instance, in ascending doses will produce in the macac monkey first depression of activity, then catalepsy, then a state resembling mania, and finally epilepsy (Richter and Paterson, 1931). Again, Gjessing (1939) has shown that recurrent catatonia can result from faulty protein metabolism.

Although such reaction patterns can sometimes be produced by drugs, it is of course usual for environmental stress to be a factor in their causation. The particular morbid reaction pattern adopted depends no doubt to a considerable degree on heredity, but imitation and suggestion can in some cases be the determining cause as shown by epidemics of hysteria in the Middle Ages or by the fact that the American negro shows different clinical pictures from his African cousin (Carothers, 1947).

If, therefore, the physiological basis of a commencing psychosis consists of a particular "set" or pattern of the nervous system, it is necessary to attempt immediately to alter this "set" by these electrical means. If the stupor, melancholia, mania or severe anxiety is allowed to continue, the condition may become intractable, or some complication such as suicide, inanition or intercurrent disease may ensue.

The electric current does not, we suppose, effect a recovery merely by its convulsant action, but by the autonomic changes which occur during the coma which accompanies and succeeds the convulsion. This perhaps explains why electronarcosis is more effective than electroshock.

The passage of an electric current is not merely a way of frightening the patient at the conscious level, like throwing a broody hen into a pond. It is true that the ancients thought they cured some madmen by throwing them into the sea from a cliff. Medieval monks held the heads of the insane under water till the priest had recited the *Miserere*. Erasmus Darwin spun them round in a revolving chair, and at Bethlem the patients were made to fall through a trapdoor into a cold bath. In the present treatment, however, the patient is usually first anesthetized and the treatment is carried out as stated entirely at the unconscious level. There is therefore no question of the treatment taking effect by the patient being subjected to conscious fear.

If this view is correct, then it is imperative to treat these patients as soon as the morbid state is manifest, a fact which is borne out by the higher proportion of successes with early psychotic cases. The time for rest and psychotherapy in these severe cases is after the electrocerebral treatment and not before. Many breadwinners who have broken down with depression and exhaustion have in the past been merely sent for a holiday to recover. The depression, however, has continued and they have been no better on their return, and in many cases they have lost their jobs. If they have electrocerebral treatment first, they enjoy their holiday and return to work quite well.

Some psychiatrists still hesitate to carry out these treatments at an early stage in patients who are obviously too ill for psychotherapy, because of possible injury to their brains. It is a fact, nevertheless, that in the hundreds of cases treated no complaint has been made by any patient or his relatives of any serious side-effect of the treatment.

We are still unable to explain why patients look and feel so much better after a few treatments, or why chronic skin diseases should clear up. Cerletti, for instance, told me that he effected a recovery in 14 out of 16 cases of psoriasis by means of electroshock. His theory that the brain develops a specific substance when threatened with approaching death is still unproved. It may be, however, that these remarkable changes are effected in part by endocrine means, particularly through the pituitary.

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With regard to the schizophrenic groups the question of diagnosis immediately arises, but I have endeavoured to exclude the atypical cases which, although they exhibit evidence of schizophrenic reaction, were probably more allied to either manic-depressive or confusional states.

METHOD

As regards the method, I have nothing to add to the description already given except to confirm that if the technique is carried out properly the patient does not receive any unpleasant sensations. We have now given approximately 2,500 treatments and, except in the paraphrenic group, no patient has refused to continue treatment and there has certainly been no apprehension, indeed many impartial observers have commented upon the cheerful and composed manner of patients awaiting, let us say, their twentieth treatment. Especially in cases of schizophrenia, it is essential to give at least thirty treatments, before assuming that the therapy is not producing the desired response. In the present series, the average number of treatments per patient has been twenty.

RESULTS

When we come to results, I am giving the following without comment as it is of course much too early to draw any definite conclusions: of the 70 schizophrenics treated, complete remissions were produced in 44%, social recoveries in 17%, social defects in 8%, while 16% were improved in hospital and in 14% no improvement was obtained (Table I). This group includes 10 children under the age of 16 who had been sent to us from various parts of the country. I think that it would be better to omit these children when considering

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Tietz reports 9 recoveries out of 13 cases of chronic severe psychoneurotics.

RATIONALE OF ELECTRONARCOSIS

I should like to add a few words about the theoretical mode of action of electrocerebral treatment. Adolf Meyer's doctrine of reaction types has proved on the whole to be a valuable one. He speaks, for instance, of the catatonic, the manic, the melancholic, or the chronically anxious patient, as having reacted to environmental stress by adopting a special type of reaction. Meyer thought of this reaction type as being modifiable by treatment such as rest, or by withdrawing the patient to the quiet of hospital under a sympathetic and understanding physician who could influence him at the conscious level.

The remarkable and unexpected success, however, of these recent physiological treatments in the psychoses or intractable psychoneuroses suggests that we must visualize the morbid reaction type as depending on a particular reaction pattern or "set" at the autonomic level of the nervous system, for they act below the level of consciousness.

It has been found that such reaction patterns may be produced experimentally by certain drugs. Bulbocapnine, for instance, in ascending doses will produce in the macac monkey first depression of activity, then catalepsy, than a state resembling mania, and finally epilepsy (Richter and Paterson, 1931). Again, Gjessing (1939) has shown that recurrent catatonia can result from faulty protein metabolism.

Although such reaction patterns can sometimes be produced by drugs, it is of course usual for environmental stress to be a factor in their causation. The particular morbid reaction pattern adopted depends no doubt to a considerable degree on heredity, but imitation and suggestion can in some cases be the determining cause as shown by epidemics of hysteria in the Middle Ages or by the fact that the American negro shows different clinical pictures from his African cousin (Carothers, 1947).

If, therefore, the physiological basis of a commencing psychosis consists of a particular "set" or pattern of the nervous system, it is necessary to attempt immediately to alter this "set" by these electrical means. If the stupor, melancholia, mania or severe anxiety is allowed to continue, the condition may become intractable, or some complication such as suicide, inanition or intercurrent disease may ensue.

The electric current does not, we suppose, effect a recovery merely by its convulsant action, but by the autonomic changes which occur during the coma which accompanies and succeeds the convulsion. This perhaps explains why electronarcosis is more effective than electroshock.

The passage of an electric current is not merely a way of frightening the patient at the conscious level, like throwing a broody hen into a pond. It is true that the ancients thought they cured some madmen by throwing them into the sea from a cliff. Medieval monks held the heads of the insane under water till the priest had recited the Miserere. Erasmus Darwin spun them round in a revolving chair, and at Bethlem the patients were made to fall through a trapdoor into a cold bath. In the present treatment, however, the patient is usually first anaesthetized and the treatment is carried out as stated entirely at the unconscious level. There is therefore no question of the treatment taking effect by the patient being subjected to conscious fear.

If this view is correct, then it is imperative to treat these patients as soon as the morbid state is manifest, a fact which is borne out by the higher proportion of successes with early psychotic cases. The time for rest and psychotherapy in these severe cases is after the electrocerebral treatment and not before. Many breadwinners who have broken down with depression and exhaustion have in the past been merely sent for a holiday to recover. The depression, however, has continued and they have been no better on their return, and in many cases they have lost their jobs. If they have electrocerebral treatment first, they enjoy their holiday and return to work quite well.

Some psychiatrists still hesitate to carry out these treatments at an early stage in patients who are obviously too ill for psychotherapy, because of possible injury to their brains. It is a fact, nevertheless, that in the hundreds of cases treated no complaint has been made by any patient or his relatives of any serious side-effect of the treatment.

We are still unable to explain why patients look and feel so much better after a few treatments, or why chronic skin diseases should clear up. Cerletti, for instance, told me that he effected a recovery in 14 out of 16 cases of psoriasis by means of electroshock. His theory that the brain develops a specific substance when threatened with approaching death is still unproved. It may be, however, that these remarkable changes are effected in part by endocrine means, particularly through the pituitary.

CONCLUSION

With regard to electronarcosis and kindred treatments, I believe that we are only at the beginning. At the present time the following investigations are being carried out at the West London Hospital or elsewhere: Psychological tests before and after treatment; blood-pressure investigations, including that of the retinal artery, intra-arterial blood-pressure, blood and cerebrospinal fluid changes, and changes in the electro-encephalogram.

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The second case which I should like to describe is that of a young man of 20, who while serving in the Army in 1944 began to express strange ideas regarding his body, and stated that he was slowly being devoured by insects. Apparently no one paid much attention to this delusion and he was able to continue to serve until June 1946 when he was released to take up essential work on the land. His mother, however, noted that during his period in the Army he had become increasingly suspicious, difficult and had lost all his friends. When he came home on leave he went for long-walks on his own, whereas previously he had enjoyed the company of his contemporaries. When he started work on the farm his workmates thought that he was very peculiar and stated that he would stop work for long periods and gaze at the sky. One day in August 1946 he drove his tractor into a ditch and immediately telephoned his mother, telling her to destroy all her ration and clothing books as the Government had decreed the end of all rationing. He returned home looking dishevelled and behaved in a most peculiar fashion. His mother called the local doctor and I was asked to see him. On examination he was a well-built lad who was mildly suspicious, reticent, self-absorbed and obviously only just able to retain contact with reality. He said that he heard various voices speaking to him and that "his mind was in a whirl" as he was commanded to do so many things at the same time. Emotional response was entirely lacking and he was quite unperturbed when questioned about the episode with the tractor. He was completely devoid of insight and stated that he was perfectly well, although the insects had been eating away at his body over a period of years. He also admitted that he had not been able to write letters for several months and his mother produced some completely incoherent, rambling and disconnected notes which he had written to her. During observation in hospital he proved to be very solitary, asocial, self-absorbed and would stand for long periods gazing into space. It was impossible to occupy his attention. Treatment by electronarcosis was commenced. After the first three treatments there was a remarkable improvement in his condition and he became bright, cheerful, sociable and asked to be given some work to do. He was, however, extremely childish and immature but after a further three weeks, during which time he had a total of fifteen treatments, he settled down very well and was able to apply himself diligently to various forms of occupational therapy. He left hospital three months after admission and had then remained completely symptom-free for two months. It was suggested that he was fit to take up further employment on a farm and he did this, but after a few months he decided that he would rather undertake office work of some description. He applied for his release from the land and just over a year ago obtained a post as a librarian. His employers are very satisfied with his services and he has been taken on to the permanent staff. There is no trace of any psychotic reaction and he appeared a perfectly normal young man.

A third case was that of a pharmacist, aged 33, suffering from hebephrenic schizophrenia. He had exhibited a gradual personality change over a period of years and finally gave up a good job and travelled about the country in an aimless fashion. He was vague in manner, dreamy, absent-minded and his conversation was bizarre and irrelevant. He said, for instance, "They tell me that I have made love to a lady doctor here and have taken a negro to America". That is not true for he has a perfectly good wife. He was hallucinated auditorially and walked up and down muttering to himself. After an unsuccessful attempt at treatment by electro-convulsive therapy he was given twelve electronarcosis treatments and a complete remission was produced. He has been back at work for over a year.

In many cases of schizophrenia, especially in hebephrenic and paranoid types, the treatment has the effect of activating the psychosis and these patients may become wildly excited, impulsive and violent. In such cases we have found it of benefit to give intensive electro-convulsive therapy until sufficient plasticity can be obtained to proceed with electonarcosis.

As might have been expected, the atypical schizophrenics responded extremely well to treatment by electonarcosis and a complete remission was produced in 14 out of the 15 cases, the fifteenth being a social recovery. It is probable that electro-convulsive therapy would have produced a similar result.

The 10 paraphrenics responded quite well to treatment and evidence of hallucinosis soon disappeared. These patients became less suspicious, lost their delusions and were apparently well after a course of treatment. On the other hand, we found that this paraphrenic group tended to refuse the treatment. I do not think this is to be wondered at, as it is asking the impossible in expecting a suspicious paranoid patient to accept the placing on of the head-band and the other preliminaries to treatment on several occasions during the week when he has no insight whatsoever into his condition. In St. James Hospital we admit a very

TABLE I.—ELECTRONARCOSIS IN SCHIZOPHRENIA

	Total	Degree of recovery as percentages				
		A	B	C	D	E
Adults and children	70	44	17	8	16	14
Adults alone	60	52	20	10	10	8

A Complete remission. B Social recovery. C Social defect.
D Improved in hospital. E No improvement.

the general results as the prognosis in all cases was hopeless from the start. In Portsmouth we have had the opportunity of treating a considerable number of cases of schizophrenia in children. I am sorry to say that we have not yet discovered a method of treatment which produces any material change in the condition. If, therefore, we consider the adolescent and adult group of schizophrenics, the total number being 60, we find that remissions were produced in 52%, 20% were social recoveries, 10% social defects, 10% improved in hospital and 8% not improved. I would point out that among the patients remaining in hospital, approximately 6% should be classed as family invalids as they merely continue as in-patients for social reasons.

The duration of the illness is of course an important factor and we find that of the 7 patients with a history of under one year, a complete remission was produced in all. This 100% recovery rate is of course due largely to coincidence. In 17 patients with a duration of illness under two years, 15 recovered and 2 were social recoveries. Out of 40 patients with a history of under five years, 60% recovered, 20% socially recovered, 7% social defect, 10% improved in hospital and 2% not improved. The duration of the follow-up has again been insufficient but in no case has it been less than three months; 40 of the cases have been followed up for periods ranging from a year to twenty months. None of those noted as "recovered" have relapsed, none of the social recoveries or defects have had to be readmitted to hospital, but 3% of those noted as improved in hospital have relapsed (Table II).

TABLE II.—ELECTRONARCOSIS IN SCHIZOPHRENIA

Results According to Duration of Illness (Adults)

	Total	Degree of recovery as percentages				
		A	B	C	D	E
Less than one year	7	100	—	—	—	—
Less than two years	17	88	12	—	—	—
Less than five years	40	60	20	7	10	2
More than five years	20	34	20	15	10	20

A Complete remission. B Social recovery. C Social defect.
D Improved in hospital. E No improvement.

In the diagnostic categories, the treatment appears to have little effect on simple types but some remarkable results have been obtained in hebephrenics. Variable responses occurred among catatonic types but there is little doubt that paranoid types on the whole respond well. This is in keeping with the findings of Tietz (1946 and 1947), Medlicott (1947) and Paterson (1948).

I would like now to give examples of actual cases, showing the response produced by the treatment.

The first is that of a nurse aged 25, who was admitted to St. James Hospital in October 1946. There was a history of some six months during which time she had become increasingly solitary, withdrawn from reality and apparently had frequent outbursts of meaningless laughter. The previous history had been very good and as far as can be ascertained there was little in the way of environmental stress to account for the onset of the condition. On admission she appeared dull, vacant, self-absorbed and exhibited various mannerisms. Her gait was peculiar and she dipped down as if curtsying at every few steps. While talking she continually moved her dentures up and down and frequently grimaced. There was evidence of considerable blocking and vagueness of thought and she expressed nihilistic ideas stating that her body was dead. She was obviously hallucinated auditorially and would frequently turn her head and reply to the voices. She exhibited a marked incongruity of affect and would say that she wished to die and then laugh and giggle in an uproarious fashion. There was no trace of depression and no real confusion. After the second treatment she was still very suspicious, and stated that her body had all gone and that only a shell was left. She was still hallucinated auditorially and stated that she was carrying on a conversation with her fiancé in Scotland. After the fourth treatment she became very much brighter and there was indeed a sudden improvement. She began to take a little interest in her surroundings and asked the nurse to send home for her dancing shoes. After the sixth treatment she started helping in the ward. There was no evidence of hallucination, but she tended to be somewhat elated in mood. After the

eighth treatment she was still rather elated, but she was making contacts very well and entertained other patients with tap and ballet dancing. After the eleventh treatment she was well occupied in the ward and interested. She had gained weight and had improved considerably. One week after the last treatment she was transferred to a convalescent villa. She was still friendly, cheerful and was working quite well but was rather untidy and, for instance, her methods of bed-making left much to be desired. After a further two weeks she began to evince considerably more interest and care in her personal appearance. Three weeks later she was taking much more responsibility and she was then allowed full parole and proved to be useful in shopping for other patients. She remained in hospital for two and a half months and during the remainder of that period there was no sign of any relapse. After a short holiday she returned to work at her hospital and has remained perfectly well for the past eighteen months.

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large number of paraphrenic cases during the year; for instance, last year over 250 cases were treated as in-patients. We have found that intensive electro-convulsive therapy produces very good results and there seemed to be no benefit in using electronarcosis.

Of the 15 cases of psychoneurosis, 12 were suffering from anxiety states and in the remainder obsessional features predominated. The treatment was employed merely as an adjuvant to psychotherapy and was most useful in dealing with panic reactions. I would like to mention only one case to illustrate this point—that of

a 40-year-old solicitor whom I have treated for impotence of eighteen years' duration. This man had many worries in regard to his professional work and when I saw him first he complained of many of the somatic equivalents of anxiety. I felt that it was hopeless to try and treat the underlying condition without modifying the acute state to some extent. The exhibition of mild sedatives, such as seconal, did little to help and so I decided to employ electronarcosis. As he could not afford time to come into hospital I gave him eight treatments at two-day intervals as an out-patient. The result was excellent and at the end of a fortnight he had lost all trace of anxiety and was calm, composed and symptom-free. It has since been possible to cure the underlying condition.

Personally I am not in favour of giving electronarcosis—or electro-convulsive therapy—to out-patients, unless in exceptional circumstances. There is no doubt, moreover, that although the degree of confusion produced by electronarcosis is considerably less than that found after electro-convulsive therapy it would appear that a sudden brief amnesic state may occur as the result of the cumulative effect of treatment. In this connexion it may be of interest to note a condition which occurred in the patient to whom I have just referred. Two nights after the last treatment he attended a dance and although he himself maintains that he had only two small whiskies, and this is confirmed by various members of his party, he was unable to remember several salient events that had occurred during the evening.

The 10 melancholics responded very well to treatment by electronarcosis, but one would have expected electro-convulsive therapy to produce similar results. On the other hand, we have used the modified method in treating a number of elderly melancholics of varying aetiology, not included in this series. The results have been comparable to those produced by electro-convulsive therapy, but electronarcosis has the benefit of being a much smoother form of treatment and one has certainly more confidence in applying it to the elderly patient.

The modified method is of use in any case where treatment by electro-convulsive therapy would be applicable. In this case the usual *Glissando* rise (Tietz *et al.*, 1946) to 180 ma. is employed. The current is allowed to remain at this level for thirty seconds and is then reduced very slowly, to zero, the actual speed being gauged by the response of the patient. The desired result is to eliminate practically all trace of the clonic stage. At the end of approximately one minute from the commencement of treatment the current is terminated. This is certainly a much more elegant form of treatment as the convulsion is modified to such an extent as to be unrecognizable.

On the basis of these results, and of two years' experience of the method, I think that one can reasonably claim that electronarcosis forms a useful addition to our armamentarium. It certainly does seem to produce some effect in schizophrenia—all the remissions which we have obtained cannot have been coincidental and spontaneous, but only the passage of time will allow us to assess the true value of the treatment.

I am indebted to Dr. Thomas Beaton, Physician-Superintendent, St. James Hospital, Portsmouth, for permission to carry out the original experimental work, to use the case material and to publish these results.

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The modification in technique which we have worked out with this apparatus is designed to ensure satisfactory oxygenation of the patient throughout the course of the electronarcosis. Insufflation with oxygen in the later stages of the electronarcosis is difficult because of spasm of the glottis, which manifests itself as the inspiratory stridor. In our technique this is considerably reduced by partial curarization of the patient. Three minutes before the electronarcosis is started the anaesthetist gives an intravenous injection of pentothal sodium 0.3 gramme to 0.4 gramme, plus atropine 1/60 grain and *d*-tubocurarine 12 mg. to 15 mg. He immediately afterwards commences the administration of pure oxygen and continues this throughout the treatment. The amount of curare given is not sufficient to prevent the muscular movements which are an important sign of the depth of the electronarcosis, but damps down any convulsive or preconvulsive movements which might produce fractures, and also causes sufficient relaxation of the vocal cords to allow of adequate oxygenation.

Occasionally, when the initial current dosage is not correctly estimated, there is a delay in the reappearance of the patient's spontaneous respiration. With our technique this need not cause anxiety as the patient can be kept pink by insufflation with oxygen by means of intermittent manual compression of an ordinary anaesthetic bag. On several occasions the patient has been kept in a satisfactory state of oxygenation despite the fact that he did not breathe spontaneously throughout the whole seven minutes of the electronarcosis.

In addition, the pentothal injection removes any apprehension due to the curarization, and also is a safeguard against the troublesome complication of an inadequate electronarcosis, of which the patient preserves a partial memory.

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The literature on electronarcosis and anaesthesia is very extensive and dates back to the last century but there seems little agreement as to fundamentals. Obviously, if the clinical results are satisfactory there is no more to be said from the physiological point of view, unless we can provide some rigorous explanation for the therapeutic action, but there is some hope that a true electronarcosis may be produced by other means, involving the use, perhaps, of a more intricate stimulation procedure and we are, at the moment, commencing experiments on these lines. It will be of particular interest to discover whether such a system is better or worse clinically, since it may well be that the therapeutic action does in fact depend primarily upon over-stimulation, exhaustion and reconditioning, rather than upon induced repose of a more nearly natural character.

Dr. T. F. Main: I hope we shall not be dismayed by the thought that social recoveries are of doubtful value. It is true that the half-improved and discharged patient does not make an ideal parent or mate, nor even a good uncle or aunt. It is true also that they must act as foci of psychopathic infection in the community. But these things are nothing new. We have always had social recoveries discharged from psychiatric hospitals and we are not worse off than before. But of course we are not better.

The descriptions we have heard of the technique of electronarcosis are a tribute to the skill and objectivity of the speakers. It would be wise, as they say, to be cautious about the interpretation of results. It is plain that many of their patients got better during the treatment, but it is not plain that they got better because of it, or in spite of it, or merely incidentally. There are, for instance, no controls. And the statistics of older psychiatrists who practised before the days of physical treatment do not provide us with good controls. Even twenty years ago many patients got better without the modern physical treatments. Up to then, early, mild psychiatric illness tended to be nursed at home for a long time, and many spontaneous recoveries took place. Mental hospitals did not admit in the same numbers as to-day the kind of cases which would remit early. The patients had been ill longer and therefore often more severely. Further, it cannot be sufficient to establish a control series merely by giving a number of patients no treatment. Electronarcosis, as we have seen this afternoon, raises enormous interest and considerable anxiety in doctors and nurses. The patient undergoing the treatment is surrounded with an atmosphere of excitement, care and unremitting attention, different from that which would be given to a patient who is having no physical treatment. A general emotional atmosphere of skilled care and devoted daily interest has great therapeutic value in itself, and in itself may be the significant therapeutic agent for many patients. This is not to decry physical treatments, for if they are the price the patient must pay for replacing the despair and apathy about recovery that was fairly common in mental hospitals up to a quarter of a century ago by enthusiasm, concern, interest, and intense optimistic devotion, then the patient would be surely glad to pay it.

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large number of paraphrenic cases during the year; for instance, last year over 250 cases were treated as in-patients. We have found that intensive electro-convulsive therapy produces very good results and there seemed to be no benefit in using electronarcosis.

Of the 15 cases of psychoneurosis, 12 were suffering from anxiety states and in the remainder obsessional features predominated. The treatment was employed merely as an adjuvant to psychotherapy and was most useful in dealing with panic reactions. I would like to mention only one case to illustrate this point—that of

a 40-year-old solicitor whom I have treated for impotence of eighteen years' duration. This man had many worries in regard to his professional work and when I saw him first he complained of many of the somatic equivalents of anxiety. I felt that it was hopeless to try and treat the underlying condition without modifying the acute state to some extent. The exhibition of mild sedatives, such as seconal, did little to help and so I decided to employ electronarcosis. As he could not afford time to come into hospital I gave him eight treatments at two-day intervals as an out-patient. The result was excellent and at the end of a fortnight he had lost all trace of anxiety and was calm, composed and symptom-free. It has since been possible to cure the underlying condition.

Personally I am not in favour of giving electronarcosis—or electro-convulsive therapy—to out-patients, unless in exceptional circumstances. There is no doubt, moreover, that although the degree of confusion produced by electronarcosis is considerably less than that found after electro-convulsive therapy it would appear that a sudden brief amnesic state may occur as the result of the cumulative effect of treatment. In this connexion it may be of interest to note a condition which occurred in the patient to whom I have just referred. Two nights after the last treatment he attended a dance and although he himself maintains that he had only two small whiskies, and this is confirmed by various members of his party, he was unable to remember several salient events that had occurred during the evening.

The 10 melancholics responded very well to treatment by electronarcosis, but one would have expected electro-convulsive therapy to produce similar results. On the other hand, we have used the modified method in treating a number of elderly melancholics of varying ætiology, not included in this series. The results have been comparable to those produced by electro-convulsive therapy, but electronarcosis has the benefit of being a much smoother form of treatment and one has certainly more confidence in applying it to the elderly patient.

The modified method is of use in any case where treatment by electro-convulsive therapy would be applicable. In this case the usual *Glissando* rise (Tietz *et al.*, 1946) to 180 ma. is employed. The current is allowed to remain at this level for thirty seconds and is then reduced very slowly, to zero, the actual speed being gauged by the response of the patient. The desired result is to eliminate practically all trace of the clonic stage. At the end of approximately one minute from the commencement of treatment the current is terminated. This is certainly a much more elegant form of treatment as the convulsion is modified to such an extent as to be unrecognizable.

On the basis of these results, and of two years' experience of the method, I think that one can reasonably claim that electronarcosis forms a useful addition to our armamentarium. It certainly does seem to produce some effect in schizophrenia—all the remissions which we have obtained cannot have been coincidental and spontaneous, but only the passage of time will allow us to assess the true value of the treatment.

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Section of Laryngology

President—A. J. WRIGHT

[May 7, 1948]

Infra-Orbital Neuralgia

By G. C. KNIGHT

THERE are frequent points of contact between the specialities of Oto-rhino-laryngology and Neurosurgery. The object of this communication is to examine one facet at which our specialities overlap—namely that of pain in the territory of the trigeminal nerve which may occasionally be deceptive and lead to difficulty in diagnosis and treatment.

The trigeminal nerve runs a long course and there is a very close association between its branches and the nasal air cells. Occasionally the sphenoidal air sinus may extend as far as the semilunar ganglion or foramen ovale, and it is a fact that the introduction of cocaine into the sphenoidal sinus may produce complete trigeminal anaesthesia, indicating how thin a layer of dividing bone separates the sinus from the nerve.

The close relationship of the sphenopalatine ganglion to the nasal mucosa is also remarkable; hence it is that certain cases of trigeminal pain occasionally have their origin in acute intranasal disease, but it is also true that atypical forms of primary trigeminal neuralgia may closely simulate the symptoms of primary intranasal suppuration.

It has been my experience that in the majority of cases intranasal operations are not followed by chronic pain and that many of those patients who suffer from persistent pain after nasal operations do so, not on account of some unrelieved condition in the nose, but from the persistence of a state that was present prior to operation which may occasionally be a psychalgia or atypical neuralgia that was mistakenly diagnosed as arising from intranasal causes.

The leading feature of psychalgic pain is that it is constant. Pain that is unremitting, that never leaves the patient, that changes in form but never in severity is always suspect, for true pain of organic origin must wax and wane as the causative disease varies in intensity; it is sometimes better and sometimes worse, whilst typical or atypical trigeminal neuralgia occurs in characteristic paroxysmal outbursts. One should always beware of the patient with a distressing background or with little responsibility, ample means, and no vital interests who complains of pain that never leaves her.

With this passing reference to psychalgia it is proposed to confine the remainder of this discussion to two subjects, namely, infra-orbital neuralgia and sphenopalatine neuralgia, each of which may occur as primary lesions independently of nasal infection and yet may simulate the pain symptomatology of antral disease or affection of the deeper air cells. With this object it is necessary to review the pathways for the conduction of pain stimuli from the paranasal regions.

The trigeminal nerve is the only pathway for the conduction of pain from the nasal air cells. I do not believe in the existence of sympathetic pathways which can produce pain in the head or in the paranasal region. It is true that referred pain in the *neck and shoulder* may occasionally be attributed to reference through the sympathetic system, but after a complete section of the trigeminal nerve it is impossible to elicit pain in the nasal region by traumatizing the nasal mucosa although the sphenopalatine ganglion and vidian nerve are still intact. Painful sensations that continue after a sensory root section are either psychalgic in origin or attributable to the escape of a few fibres in the sensory root which has left the trigeminal pathways partially intact as a result of an incomplete operation.

The major portion of the trigeminal supply from the nose is conducted in the second division of the trigeminus, only a relatively small proportion returning in the first division. The first or ophthalmic division passes through the sphenoidal fissure conducting pain

the previous physical treatments has justified the high hopes placed on it after its innovation. The later figures have not been as good as the earlier enthusiastic ones. It occurs to me that all of these treatments are either dangerous or dramatic, and while nurses and doctors were learning the techniques, they themselves were anxious and uneasy on behalf of the patients, giving daylong skill and unremitting interest, supporting the patient with all the professional anxiety they could command. Since the techniques of these treatments have been established, and they have become safer and more "ordinary", there is less excitement about them. They have become conventionalized and routine and comparatively dull. This meant also a change in the attitude to the patient undergoing the treatment. There is less anxiety for the patient, and less therapeutic effect. This has occurred with continuous narcosis, electro-convulsive therapy, and insulin coma. To-day's papers, to the credit of the authors, show the same intensity and concern for the patient and the treatment method. When the technique of electronarcosis becomes clearly established and of less concern to the therapists, the atmosphere round the patient will, of course, change in the same way as with the other physical treatments, and we must hold our hand before writing the final assessment of results. But we need not despair. Electricity is a wonderful thing and human ingenuity knows no bounds. We may be sure that when electronarcosis is familiar and undramatic, new dramatic and perhaps dangerous forms of using electricity for patients will arise and will stimulate again medical excitement and nursing devotion, and the patients will continue to benefit from an active atmosphere of sincerity and minute-by-minute concern on their behalf. And if we continue to get earlier and milder cases admitted to our mental hospitals, the published figures will continue to improve.

It may be that electronarcosis has direct and specific values of its own, but these are at present obscure and unproven and I doubt whether theorizing about "normalizing electrical patterns of the brain" is justified. Our tribute must be to the authors' skill and scientific detachment and one hopes that research into the effects of electricity upon nervous tissue will continue.

Electronarcosis must also be considered as a total experience to the patient with a significance of its own for him. I have been impressed by observing the behaviour of a patient who in his past life, particularly in his career, where he persistently refused promotion and undertook unrewarding but dangerous work, showed himself to have deep and quite unconscious masochistic tendencies. He liked electronarcosis and loved the doctors who gave it to him and who admired his spirit of eagerness for the treatment. He made one complaint on recovering from his fourth treatment—"That was nothing. Too easy; in fact it may seem odd but I am a little bit disappointed". The point here is that in unpleasant experiences there are sometimes deep unconscious satisfactions. We know, too, that the best results of electronarcosis are plainest in those people who have intrapunitive wishes extending to suicidal ideas—namely, in depression. We should be wise to acknowledge the possibility that by electronarcosis we sometimes satisfy a need which has psychological rather than electrical values. Masochism is a fairly universal human component and it is usually deeply unconscious. When unpleasant experiences are given by medical authority and administered with kindness, devotion and care, we should not be tempted to think in terms of electricity only.

In post-herpetic neuritis the pain is usually widespread and involves a greater area than the territory of the infra-orbital nerve. Infra-orbital avulsion is therefore seldom to be considered in these cases, but I would recall that I have had experience of two patients in whom infra-orbital avulsion alone has succeeded in curing the pain. I would like to mention especially the case of a doctor in whom pain was experienced in the infra-orbital territory in the region of the canine tooth, in the lower lid of the eye and in the whole of the upper cheek, and also deeply behind the eye and deeply in the nose. The presence of pain in the eye and within the nose made me suspect that infra-orbital avulsion would fail, but in view of the great age and frail physique of the patient, who was forced to take large doses of opiates, it seemed that a small operation under local anaesthesia should be tried. A particularly large portion of the nerve was removed at operation and complete relief of pain was obtained except for some sore discomfort that continued in the nose in the region of a perforation of the nasal septum which received its supply through branches of the nasopalatine division.

I find that infra-orbital avulsion is ineffectual as a means of relieving chronic pain resulting from infection of the paranasal sinuses, presumably on account of the wider area of their nerve supply, excepting in those cases where pain is confined entirely to the region of the maxilla and canine fossa and upper teeth. Deep pain that is experienced in the region of the eye, the side of the nose, and hard palate requires an operation on the sensory root of the trigeminus in order to interrupt the important fibres that are supplied from the sphenopalatine ganglion.

SPHENOPALATINE NEURALGIA

The sphenopalatine or nasal ganglion is a small triangular reddish grey body with the apex downwards, situated in the upper portion of the sphenomaxillary fossa—lying beneath the second division of the trigeminal nerve—in close proximity to the nasal mucosa—at a depth varying in different dissections from 1–2 to 7–9 millimetres. It may occasionally occupy a direct submucous position or be replaced by two separate and smaller ganglia which are related to the sphenopalatine nerves.

The structure of the ganglion consists of sensory branches of the trigeminus and motor branches of the facial that are prolonged through its substance together with sympathetic ganglia cells which occupy a posterior position in the ganglion at its junction with the vidian nerve.

The sensory roots of the ganglion consist of two or three stout filaments of the sphenopalatine branches which pass through the ganglion to the nose and palate without being in any way incorporated with the cells of the ganglion mass.

The motor root is supplied by the great superficial petrosal from the geniculate ganglion of the facial. This nerve also conveys taste fibres from the anterior two-thirds of the tongue which have passed via the chorda tympani to the geniculate and thence through the great superficial petrosal to Meckel's ganglion and will finally join the second division of the trigeminal nerve.

The sympathetic root of the ganglion consists of the great deep petrosal branch from the carotid plexus which joins the great superficial petrosal beneath the gasserian ganglion in the region of the foramen lacerum medium to form the vidian root.

The branches of distribution have been already referred to, but we may emphasize again that the trigeminal fibres of the sphenopalatine nerves are to be regarded as the splanchnic components of the trigeminus supplying internal structures as contrasted to the somatic peripheral branches of the first, second and third divisions. The pain arising from involvement of these branches differs from that of ordinary trigeminal neuralgia both in distribution and type. The distribution of the pain corresponds closely to the branches of distribution of the ganglion and also to the territory of the infra-orbital nerve.

In sphenopalatine neuralgia pain is experienced in the alar region of the nose and spreads laterally into the cheek and up to the infra-orbital region. At the height of the paroxysm the pain is also experienced deep inside the nose and in the hard palate and gums. The pain is of a continuous burning type and may last for twenty minutes or for many hours in each paroxysm, tending to spread to involve wider and wider areas during the attack; it is often associated with a sensation of tension in the affected area; it differs from trigeminal neuralgia in the longer duration of the paroxysms. Occasionally the symptoms will include loss of taste in the anterior two-thirds of the tongue. Physical examination, which is usually entirely negative, may reveal a slight reduction of sensation over the soft palate on the affected side and of the pharynx as far down as the tonsil. Vasomotor and secretory disturbances are occasionally observed in association with the attack, consisting of reddening of the conjunctiva and profuse secretion of tears. These phenomena have given rise to speculation as to the part that the sympathetic pathways may play in the causation of this pain,

sensations from the eyeball and lacrimal gland, from the upper portion of the nasal mucosa, and the skin of the upper eyelid and mid-line of nose, and from the forehead and scalp as high as the vertex.

The second or maxillary division passes from the foramen rotundum across the sphenomaxillary fossa to the infra-orbital canal. In the sphenomaxillary fossa it gives off its main supply to the paranasal sinus, being connected to the sphenopalatine ganglion of Meckel by two or three stout filaments, the sphenopalatine nerves. These constitute the sensory roots of the ganglion and pass directly from the maxillary division to the upper border of the ganglion, passing through the ganglion without forming contact with the ganglion cells, to be continued as the important sensory branches of distribution, which together innervate the greater portion of the nose, nasopharynx and accessory air cells, the area of distribution covering the nasal mucosa, except in the region of the inferior turbinate, the roof and septum of the nose, the hard palate in the region of the incisors, the sphenoid and ethmoidal air cells and the nasopharynx in the region of the fossa of Rosenmüller.

<i>Branches of distribution of sphenopalatine ganglion</i>				<i>Area of sensory distribution</i>
Ascending or orbital	{ Sphenoid Posterior ethmoids Periosteum orbit Nasal mucosa, except region of anterior and inferior turbinate Hard palate Inside of gum Tonsil and soft palate
Descending or large posterior palatine				
Accessory	
Internal or posterior, superior, nasal, nasopalatine	
Posterior or pterygopalatine	{ Posterior superior nasal fossa. Roof and septum and hard palate in region of incisors Nasopharynx fossa of Rosenmüller

These internal branches of distribution are to be regarded as the splanchnic distribution of the trigeminus as opposed to the somatic branches which, through the first, second and third divisions innervate the peripheral structures of the skin and jaws. Disturbances arising from the splanchnic territory may well have a different clinical character to similar disturbances arising in the area of somatic supply.

Anterior to the sphenopalatine ganglion the infra-orbital nerve enters the infra-orbital canal and is then distributed in branches to the wall of the maxillary antrum and to the incisor, canine and the first premolar teeth (the second premolar and molars receiving a separate supply through the posterior superior alveolar branch), and finally emerges from the infra-orbital foramen to supply the skin of the infra-orbital region. Pain arising from involvement of the infra-orbital nerve will therefore be confined to the cheek in the region of the ala of the nose, and the anterior portion of the upper alveolus, especially in the region of the canine fossa.

INFRA-ORBITAL NEURALGIA

Paroxysmal infra-orbital neuralgia occurs in two forms: It may appear as a presenting feature of trigeminal neuralgia and later spread to involve other branches of the trigeminus, or it may arise from local causes following upon dental extractions in the canine region and other operations in the region of the canine tooth, in which case the pain will remain entirely localized to the infra-orbital territory. Complete relief of pain may be obtained by infra-orbital avulsion in cases that have a local cause, but avulsion is an unsatisfactory method of treatment in trigeminal neuralgia as the pain will later extend to involve other branches.

Paroxysmal explosive attacks of pain of brief duration simulating the pain of trigeminal neuralgia may be seen in cases that have a local origin. Alternatively the pain may be continuous with exacerbations and remissions.

I recall the case of a Dutch seaman whose pain commenced following the extraction of his canine tooth. A constant pain was present in the region of extraction and in adjacent portions of the superior alveolus: there was a feeling of dull heavy pain in the cheek below the eye—an associated antral infection was suspected. The antrum was punctured, with negative results. Paroxysmal explosive outbursts of pain of great severity then commenced and occurred infrequently during the first year but later became more frequent. Complete relief followed avulsion of the infra-orbital nerve.

In other cases local pain has followed alveolectomy and in these, too, it has been possible to relieve the discomfort by infra-orbital avulsion provided that the pain was strictly confined to the region of the anterior portion of the upper jaw.

In post-herpetic neuritis the pain is usually widespread and involves a greater area than the territory of the infra-orbital nerve. Infra-orbital avulsion is therefore seldom to be considered in these cases, but I would recall that I have had experience of two patients in whom infra-orbital avulsion alone has succeeded in curing the pain. I would like to mention especially the case of a doctor in whom pain was experienced in the infra-orbital territory in the region of the canine tooth, in the lower lid of the eye and in the whole of the upper cheek, and also deeply behind the eye and deeply in the nose. The presence of pain in the eye and within the nose made me suspect that infra-orbital avulsion would fail, but in view of the great age and frail physique of the patient, who was forced to take large doses of opiates, it seemed that a small operation under local anaesthesia should be tried. A particularly large portion of the nerve was removed at operation and complete relief of pain was obtained except for some sore discomfort that continued in the nose in the region of a perforation of the nasal septum which received its supply through branches of the nasopalatine division.

I find that infra-orbital avulsion is ineffectual as a means of relieving chronic pain resulting from infection of the paranasal sinuses, presumably on account of the wider area of their nerve supply, excepting in those cases where pain is confined entirely to the region of the maxilla and canine fossa and upper teeth. Deep pain that is experienced in the region of the eye, the side of the nose, and hard palate requires an operation on the sensory root of the trigeminus in order to interrupt the important fibres that are supplied from the sphenopalatine ganglion.

SPHENOPALATINE NEURALGIA

The sphenopalatine or nasal ganglion is a small triangular reddish grey body with the apex downwards, situated in the upper portion of the sphenomaxillary fossa—lying beneath the second division of the trigeminal nerve—in close proximity to the nasal mucosa—at a depth varying in different dissections from 1–2 to 7–9 millimetres. It may occasionally occupy a direct submucous position or be replaced by two separate and smaller ganglia which are related to the sphenopalatine nerves.

The structure of the ganglion consists of sensory branches of the trigeminus and motor branches of the facial that are prolonged through its substance together with sympathetic ganglia cells which occupy a posterior position in the ganglion at its junction with the vidian nerve.

The sensory roots of the ganglion consist of two or three stout filaments of the sphenopalatine branches which pass through the ganglion to the nose and palate without being in any way incorporated with the cells of the ganglion mass.

The motor root is supplied by the great superficial petrosal from the geniculate ganglion of the facial. This nerve also conveys taste fibres from the anterior two-thirds of the tongue which have passed via the chorda tympani to the geniculate and thence through the great superficial petrosal to Meckel's ganglion and will finally join the second division of the trigeminal nerve.

The sympathetic root of the ganglion consists of the great deep petrosal branch from the carotid plexus which joins the great superficial petrosal beneath the gasserian ganglion in the region of the foramen lacerum medium to form the vidian root.

The branches of distribution have been already referred to, but we may emphasize again that the trigeminal fibres of the sphenopalatine nerves are to be regarded as the splanchnic components of the trigeminus supplying internal structures as contrasted to the somatic peripheral branches of the first, second and third divisions. The pain arising from involvement of these branches differs from that of ordinary trigeminal neuralgia both in distribution and type. The distribution of the pain corresponds closely to the branches of distribution of the ganglion and also to the territory of the infra-orbital nerve.

In sphenopalatine neuralgia pain is experienced in the alar region of the nose and spreads laterally into the cheek and up to the infra-orbital region. At the height of the paroxysm the pain is also experienced deep inside the nose and in the hard palate and gums. The pain is of a continuous burning type and may last for twenty minutes or for many hours in each paroxysm, tending to spread to involve wider and wider areas during the attack; it is often associated with a sensation of tension in the affected area; it differs from trigeminal neuralgia in the longer duration of the paroxysms. Occasionally the symptoms will include loss of taste in the anterior two-thirds of the tongue. Physical examination, which is usually entirely negative, may reveal a slight reduction of sensation over the soft palate on the affected side and of the pharynx as far down as the tonsil. Vasomotor and secretory disturbances are occasionally observed in association with the attack, consisting of reddening of the conjunctiva and profuse secretion of tears. These phenomena have given rise to speculation as to the part that the sympathetic pathways may play in the causation of this pain,

but bearing in mind the function of the great superficial petrosal nerve which is the secretomotor nerve to the lacrimal gland, the excessive tear secretion is easily understandable.

Sphenopalatine neuralgia may arise as a primary and independent condition without any associated intranasal suppuration. The syndrome is therefore by no means indicative of intranasal disease. With this qualification it is necessary in any discussion of this subject to pay tribute to the work of Dr. Greenfield Sluder for his extensive clinical and anatomical studies of the sphenopalatine syndrome. Sluder's original description of the sphenopalatine syndrome was published on May 23, 1908, in the *New York Medical Journal*, 87, 989; in it he gives an excellent description of the symptomatology:

"Occasionally it has been my lot to be consulted by patients who were in every way healthy and normal, but who suffered much of the time from headache which did not follow any of the known rules. Sometimes it was referred to behind the eyes, sometimes to the upper jaw in front, and sometimes to the hard or soft palate. Occasionally the nose was said to ache in the back, or the teeth were described as sore, or the pain was referred to the temple. Sometimes an indefinite sense of stiffness was described. These symptoms appeared from day to day, alternating one with the other, or associated two or three together. On one occasion I had them all described at once. I have seen some high grade inflammatory troubles in the posterior ethmoidal and sphenoidal sinuses, which have subsided and healed, usually within a week or two, but have left the train of symptoms, as described, in their wake, and these have continued on more or less indefinitely. This exceedingly irregular train of symptoms cannot be explained on a basis of inflammatory troubles in the accessory sinuses."

He points out the possibility of infection of the ganglion by the extension of sepsis from the nose and concludes:

"The distribution of the nerve processes of this ganglion corresponds closely with many of the regions to which pain is referred by these patients."

Sluder, in his numerous monographs, draws attention to the anatomical relationship of the sphenopalatine ganglion; he points out the close proximity of the ganglion to the sphenopalatine foramen, a relatively exposed position which he thought might lead to the passage of infection from the nose to the ganglion. He also drew attention to the fact that the sphenomaxillary fossa was related superiorly to the thin bone of the sphenoidal sinus and sphenoidal process of the palate bone, and posteriorly to the occasional prolongation of the sphenoid downward within the pterygoid process and great wing, and anteriorly to the thin posterior wall of the maxillary sinus. He maintained that infection might transude from the thin bone in this situation and lead to inflammatory changes in the ganglion with resulting pain. However, he drew attention to the fact that anteriorly the sphenopalatine ganglion was in relationship with the descending palatine artery and the sphenopalatine artery with their corresponding veins, and that these structures, together with surrounding connecting tissue, formed a protective pad which separated the ganglion by some 3 to 4 mm. from the wall of the maxillary sinus forming the anterior boundary of the fossa; a finding which he thought might explain his belief that the characteristic disturbances of sphenopalatine neuralgia were more likely to follow upon inflammation of the ethmoid and sphenoidal sinus but were not at all likely to ensue from extension of infection from the posterior wall of the maxillary antrum. Soon, however, evidence appears that even Sluder himself was beginning to doubt that all cases of sphenopalatine neuralgia were really of nasal origin.

In 1910 in a communication to the Section of Internal Medicine of the St. Louis Medical Society (*New York med. J.*, 91, 850) he described two cases of typical sphenopalatine neuralgia occurring without previous nasal sinus infection and, in 1913, twelve cases of "systemic toxic origin" (*Trans. Sect. Laryng. Otol., Amer. med. Ass.*).

It may of course be true that an infection of the ganglion might follow upon infection of the nasal air cells in the manner that Sluder suggests. This is a matter upon which I would appreciate your helpful comments in the subsequent discussion. If it is true that sphenopalatine neuralgia CAN be a complication of nasal disease, it is equally true that paroxysmal explosive attacks of sphenopalatine neuralgia may arise as a primary condition as a variant of the more usual trigeminal neuralgia occurring in patients who have never had any evidence of nasal suppuration whatsoever.

TREATMENT

In the past, many cases exhibiting the sphenopalatine syndrome have had their treatment commenced by various operative procedures on the nose, carried out in the belief that their pain arose from nasal causes. In view of the fact that a nasal origin for this syndrome is by no means proven, I would suggest that intranasal operation should be undertaken in this condition only when positive proof has been obtained of the co-existence of intranasal infection and that operations which are exploratory in character should be rigidly avoided.

Local measures designed to produce a temporary relief of pain consist of cocaineization of the sphenopalatine ganglion. The application of cocaine to the region of the sphenopalatine foramen produces a transitory effect which lasts approximately half an hour. This short period of temporary relief may succeed in abating an attack and may cut short the severe symptoms of hypersecretion of tears and excessive nasal secretion that are sometimes associated with the syndrome. Local measures of this kind can of course produce no permanent effect in those cases in which paroxysms of pain are frequently repeated.

Injection of the sphenopalatine ganglion is also an uncertain and unsatisfactory method. It is no mean feat to plant an injection directly into a structure 5 mm. in length which occupies an inconstant depth from the surface of the nasal mucosa. Many of the injections that have been performed have for this reason been merely periganglionic and have led to an exacerbation of the existing disturbance by production of scar tissue and inflammatory reaction around the ganglion itself. In other cases if certain anatomical variations are present, or if the course of the needle is not perfectly directed, quite serious injury may be caused by attempted injection. Cases are recorded of injury to the nerves lying in the sphenoidal fissure produced by a needle that was imperfectly directed from the posterior palatine canal.

Sluder's technique of using a straight needle that is introduced beneath the posterior tip of the middle turbinate 0.66 cm. from its posterior margin appears to be the safest method of approach, but the results of these measures have been extremely inconstant. The injection of solutions of 5% phenol in alcohol has had to be repeated in many cases from three to ten times. Injection may be accompanied by a considerable pain reaction after a short period of comfort, and this reaction, which is the result of inflammatory disturbances in the region of the ganglion, tends to become more and more severe each time the injection is repeated—as Sluder says: "Severe cases of this kind are not only a terrible affliction for the patient. They may also put the Surgeon at his wits' end for judgment, perseverance, and skill." I would suggest that perhaps it were better not to embark upon so hazardous a course.

I would now like to recount two cases of sphenopalatine neuralgia arising as primary disease, independently of any intranasal suppuration, that have been completely relieved by sensory root section of the trigeminus.

CASE I.—Male, aged 42, complaining of paroxysms of pain in the left side of the face which had been present for seventeen years, occurring at intervals of approximately six to seven hours throughout the whole of that time. In 1930 this patient began to experience pain: the paroxysms began just lateral to the nostril and then spread laterally into the cheek and up to the infra-orbital region. At the height of the paroxysm he would also experience pain deeply inside the left side of his nose and also on his hard palate and gums on the left side. This pain was of a continuous burning type, lasting for about twenty minutes, then subsiding gradually and leaving his face sore. His paroxysms occurred approximately every six to seven hours and were usually of the same intensity. They were brought on by going out in the cold wind but there did not appear to be any special trigger area. He stated that if he had a cold he became free from the attacks or that they became less severe. His trigeminal nerve had been injected on four occasions with some analgesia but no relief from symptoms. Examination revealed no abnormal signs in the central nervous system.

In view of the suggestion that pain of this type might be conveyed through sympathetic pathways, an attack was elicited by stimulating the posterior part of the septal aspect of the left middle turbinate. This produced symptoms clearly recognized by the patient as the earlier stages of a typical attack; they included throbbing in the area of the pain, lacrimation in the left eye and a peculiar "early" pain deep in the face which preceded the full development of pain. The left cervical and thoracic sympathetic was then injected beneath the first rib by the posterior route; five minutes later sympathetic paralysis became evident with the development of a left Horner's syndrome. The left upper limb became hot and flushed, the left-sided nasal mucosa became very congested.

Repeated stimulation of the nasal mucosa again produced exactly the same symptoms of pain with lacrimation of the left eye, and some three minutes later he had a spontaneous and typical attack of pain at a time when the sympathetic paralysis was well developed, thus indicating that sympathetic block does not modify the onset or character of the attacks. At a later date a complete sensory root section was performed and from that date the patient has had no further attacks of pain.

CASE II.—Male, aged 38. He experienced similar attacks of pain for four years and was completely relieved by a subtotal sensory root section designed to interrupt the fibres of the first and second divisions only, and in this patient also there was no evidence of any intranasal disease.

To summarize, it would appear that sphenopalatine neuralgia may occur as a variant of trigeminal neuralgia, independently of associated inflammation in the paranasal sinuses, that it is capable of complete and lasting relief by sensory root section; that the sympathetic pathways appear to play no part in the conduction of pain stimuli. It is possible that this condition may be of post-herpetic origin and comparable to herpes of the geniculate ganglion.

E. D. D. Davis said that for many years the Royal Dental Hospital had sent cases to his clinic at Charing Cross. The most common condition was alveolar pain following extraction. This was purely

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Section of Anæsthetics

President—JOHN CHALLIS

[March 5, 1948]

The Present Position of Myanesin in Anæsthesia¹

Clinical Aspects

By F. BARNETT MALLINSON

SINCE the first report on myanesin, more than a year has passed. As I indicated in it (1947*a*), that report was intended to stimulate interest in and promote the acquisition of further experience with a promising agent for the advance of the technique of curarization.

It is estimated that since then more than 10,000 administrations of myanesin have taken place. There has been much comment and a number of papers, mostly favourable, which include those of Lyall (1947), Wilson (1947), Turnbull (1947), Ballantyne (1948), and Wilson and Gordon (1948), but also one or two critical, notably those of Pugh and Enderby (1947) and Hewer and Woolmer (1947).

I do not propose to waste time in further descriptions of technique, but I think it is worth while briefly to mention a few points in connexion with the use of the drug in special operations and manœuvres.

Further experience of myanesin has confirmed my opinion that there is no combination of it with pentothal which makes it a worth-while aid to intubation under that anæsthetic. I would add that I am also confirmed in the opinion I expressed here last year (1947*b*) that there is likewise no combination of curare with pentothal for this purpose that is both effective and justifiable.

My opinion is confirmed that myanesin will abolish laryngeal spasm; but for it to be really effective the patient must be actually under anæsthesia, and not merely in the second stage.

The statement that myanesin is usually effective in first plane anæsthesia still holds good but with one notable exception. Patients who have an irritated peritoneum, such as those with perforated peptic ulcer, need anæsthesia in the second plane, to secure really good relaxation.

Generally speaking the principal field of use for myanesin remains that of abdominal surgery. Exceptions are the operation of hæmorrhoidectomy, where a combined injection of pentothal with myanesin produces a perfectly relaxed and patulous anus; and colpopræneal repairs.

I have also found myanesin useful in securing a relaxed and tranquil pharynx in tonsillectomy performed under the now widely adopted technique of pentothal and intra-tracheal gas-oxygen. The need for supplemental ether in children is thus entirely eliminated, even in young children anæsthetized without intubation in whom I have used a pentothal-myanesin mixture with satisfactory results down to the age of 3 years. In the absence of etherization this technique ensures a rapid recovery of the cough reflex because less pentothal is needed. For children I make up a mixture to 20 c.c. with pentothal 1 gramme and myanesin 1 gramme (10 c.c.). This mixture is used for a slow induction and the needle kept in the vein throughout the operation while gas-oxygen is insufflated through the Boyle-Davis gag; $\frac{1}{4}$ -1 c.c. of the mixture is added as it is needed. The same mixture is also useful for ophthalmic surgery in children under general anæsthesia, because it eliminates the tendency to sudden twitching movements which are characteristic of pentothal anæsthesia in them unless carried dangerously deep.

For anæsthesia in cesarean section, 0.25 gramme pentothal with 10 c.c. of myanesin are used for induction followed by gas-oxygen; as a result of the minimal amount of pentothal the babies are born in a satisfactory state of vigour (Table I) whilst a quiet and smooth anæsthesia for the mother under gas-oxygen only is assured.

¹The paper read by Dr. S. W. F. Underhill at this meeting will appear in *Anæsthesia*.

a local pain and he came to the conclusion that it was due to a periostitis, possibly following upon absorption of bone subsequent to extraction. The treatment was to incise right down to the bone, and that procedure was successful in a few cases only. The relief afforded by injections of novocain was temporary. These cases often occurred in nervous, anxious women.

Infra-orbital neuralgia was a rare condition and was purely subjective. There were no visible signs and he believed these cases were part of a trigeminal neuralgia and the pathology or aetiology was obscure. There was nothing in the nose that he had found to account for the pain and nothing objective in the face. The pain in the auriculo-temporal nerve from a lower molar tooth or some painful condition of the mandible was very characteristic. It spread to the ear and the side of the head, almost up to the vertex. No local cause could be found in most cases of sphenopalatine neuralgia. He considered that it was a part of trigeminal neuralgia. He had not seen sphenoidal sinus suppuration or neoplasm accompanied by sphenopalatine neuralgia.

The speaker recalled a visit he had paid to a clinic in Paris, when some cases of sphenopalatine neuralgia were shown. These patients were treated by the application of wool soaked in cocaine on the area of the ganglion. They returned regularly to the clinic for their treatment and appeared to become cocaine addicts.

Another type of case which was difficult was the patient who complained of pain near the intra-nasal antral window made in the inferior meatus by an operation. He believed that this was due to scarring involving one of the dental nerves.

J. A. Harpman, after referring to the use of cocaine on the sphenopalatine ganglion area for pain which in some cases he thought was vascular in origin, possibly sometimes with an allergic basis, said that it was now widely accepted that in some pain syndromes a peripheral interaction takes place between sensory nerve fibres subserving pain and sympathetic nerve fibres. He quoted some observers (e.g. Pollock) who, he thought, had found that sufferers from sphenopalatine ganglion neuralgia were not always relieved by cutting trigeminal nerve fibres. For these pains medical lines of treatment, such as the administration of nicotinic acid, benadryl or salicylates, frequently helpful for a while, often eventually failed to relieve. In women, sphenopalatine ganglion neuralgia was occasionally found to be worse just before a menstrual period and could then sometimes be relieved by progesterone. But by far the most satisfactory line of treatment he had yet found was cocaineization of the sphenopalatine ganglion region followed by treating it with 1% to 2% silver nitrate solution; stronger solutions were liable to be irritating and sometimes caused a temporary flare-up of the pain.

G. C. Knight, in reply, said that Mr. Davis had asked him whether he had encountered ulceration of the nose in association with sensory root section. He had seen herpetic ulceration in the nose follow this operation.

Another speaker had brought up the question of the pathway of the sympathetic as a means of conducting pain. It was perfectly true that pain could be referred through the sympathetic, but he would not accept for one moment that the persistence of pain after sensory root section necessarily meant that it had found its way back through the sympathetic. Anybody who had done trigeminal root sections would admit that he was bound to miss a few fibres occasionally. There might be just one or two fibres left but it was quite amazing what an area those fibres could supply. It seemed to him that pain in the face and palate could not be sympathetic in origin, but pain in the shoulder and neck might be a referred pain.

Film: Lesions of the Larynx

G. Ewart Martin introduced a film of lesions of the larynx prepared by Dr. Louis Clerf of Jefferson Hospital, Philadelphia, who had kindly lent the film for exhibition in this country.

The film first showed a normal larynx. This was followed by vocal nodules and papilloma of the larynx and also papilloma of the trachea coming up between the cords. Following on this there was a case of keratosis of the cords; of carcinoma of the cords and epiglottis; and of tubercle of the larynx. That part of the film which showed tubercle of the larynx was, perhaps, not so instructive because any duplication of a colour film tended to emphasize the reds and the photographs of the tubercle of the larynx did not show the characteristic pallor. Paralysis of the cords was also filmed and a very interesting case of functional aphonia, and finally injuries to the larynx.

Ewart Martin said that Dr. Clerf's film indicated a means of teaching students the appearance of the more common lesions of the larynx which was more impressive than drawings or even actual still photographs. Dr. Clerf had already published his method of filming the larynx with indirect laryngoscopy. The advantage from the teaching point of view was that it showed a mirror image of the larynx exactly as would be seen on indirect examination. It illustrated the difficulties that the student or practitioner might have in viewing the appearance and movements of the cords.

The film was also shown with the idea of stimulating those interested in cine photography to record their cases of lesions of the larynx.

The only serious worry I have encountered has been in connexion with possible hæmolytic and, as a result, possible derangement of kidney function. After over a hundred perfectly satisfactory cases, one patient (a boy aged 9 years) suddenly passed an apparently bloody urine. This was unfortunately thrown away before I could obtain it for pathological investigation. The phenomenon was not repeated and the patient made an uninterrupted recovery. The urea concentration tests before operation and five days afterwards and again a month later failed to reveal any alteration in kidney function. About this time also, following a very long and difficult hysterectomy during which severe hypotension and shock developed, another patient passed one apparently bloody urine. Again owing to poor staff work the specimen was lost (it had been reported as definite *hæmaturia*) but the patient proceeded to develop uræmia and died on the eighth day from pulmonary oedema and heart failure. The cause of this death was not satisfactorily cleared up until I was able to obtain a kidney section which I submitted to E. M. Darmady who has done such brilliant work on traumatic uræmia (1946, 1947a). He demonstrated to me conclusively that this case belonged to the traumatic uræmia syndrome, the appearances of the kidney section being typical of his classical description of "crush syndrome without crush injury", also described by Bywaters and Belsey (1942) amongst others, and a conception now well recognized. It has been considered to be due to renal anoxia following severe hypotension from hæmorrhage or shock by most workers, notably Bywaters and Beall (1941), Darmady *et al.* (1944), Macgrath, Harvard and Parsons (1945), Phillips *et al.* (1946), and Selkurt (1946). By Trueta, however, it is suggested that the condition may be due to renal ischæmia resulting from afferent stimuli (1945). The cause of death in this case then was clearly unconnected with myanesin.

It is also worthy of note that in this case pigment was conspicuous by its absence in the section, indicating that there was none in circulation and thus that there had been no hæmolytic. A second case occurred soon after this with an identical train of symptoms, also following a difficult and very prolonged shock-producing operation, for gall-stones. This patient, after remaining ill for some weeks, recovered after dialysis by Bywaters on the Kolff artificial kidney (Bywaters and Joekes, 1948). Her cardiac and general condition were much better than that of the first case. Subsequent investigations have shown only slight renal damage still persisting and I consider that this patient should undoubtedly also be labelled post-operative traumatic uræmia. After these cases imperative instructions were issued to those responsible regarding the saving of abnormally coloured urines, following myanesin injection and a number of investigations were started.

First, a series of exhaustive analyses was made of the urines of patients who had received myanesin. Two of these urines showed an apparently bloody appearance and several were very dark, as will be seen in Table II. Special emphasis was laid on the presence or absence

TABLE II.—URINE ANALYSES. MYANESIN (15 Cases)

Sex	Age	Operation	pH	Sp. gr.	Colour	Albumin	Blood (benzidine)	W.B.C.	R.B.C.	Casts	Epi-thelial cells	Presence of iron: Spectro-scope
M	46	Bilat. I. hernia	5.2	1047	Normal	Trace	—	—	—	—	—	—
F	31	R.I. hernia	5.4	1003	Normal	Nil	—	+	—	—	—	—
F	54	Ovarian cyst	4.8	1013	Normal	F. trace	—	—	—	A few	++	—
M	49	Gastrectomy	5.4	1009	Normal	F. trace	—	+	—	A few	A few	—
M	79	Intra-peritoneal close colostomy	5.2	1013	Normal	—	—	—	—	—	—	—
F	54	Bilat. F. hernia	4.8	1012	Normal	—	F. positive	—	A few	A few	+	—
M	61	Bilat. I. hernia	5.6	1016	Dark	—	F. positive	—	—	—	A few	—
M	57	R.I. hernia	4.8	1016	Normal	F. trace	—	Occasional	—	—	—	—
F	33	T. hysterect.	5.5	1008	Dark	F. trace	—	A few	—	—	—	—
F	35	Bilat. F. hernia	6.7	1015	Normal	—	—	—	—	—	—	—
F	39	Ovarian endometrioma	5.8	1009	Normal	F. trace	—	+	—	—	—	—
F	40	T. hysterect.	6.2	1015	Brownish	F. trace	Positive	+	—	—	—	—
F	52	Panhysterect.	Acid	1049	Normal	F. trace	—	+	A few	—	—	—
F	42	T. hysterect.	7.9	1015	Bloody	F. trace	Positive	—	A few	—	A few	—
F	39	Appendicect.	4.9	1007	Bloody	Positive	F. positive	A few	A few	A few	+	—

of iron in these analyses. According to Dr. F. M. Berger who performed the analyses (1947) in no case was a band denoting the presence of iron detected with the Hartridge reversion spectrocope.

Second, urea clearance estimations were carried out on a further series of patients before and five to seven days after operation, (a) after myanesin, (b) after various other anaesthetic techniques. As will be seen from Table III nothing could be concluded from this investigation

TABLE I.—CÆSAREAN SECTION (9 Cases)

Age	Special state	Labour?	Operation	Time	Breathed	Baby Cried
43	Placenta præv.	No	Classical	40 min.	5 min.	5 min.
26	—	No	Lower seg.	35 min.	1 min.	3 min.
26	—	No	Classical	35 min.	Statim	Statim
38	—	Yes	Lower seg.	47 min.	Statim	Statim
37	—	No	Lower seg.	30 min.	Statim	Statim
40	Cardiac disease	No	Classical	40 min.	Statim	Statim
44	—	No	Classical	30 min.	Statim	Statim
42	Toxæmia	No	Classical	35 min.	$\frac{1}{2}$ min.	1 min.
31	Premedicated	Yes	Lower seg.	45 min.	1 min.	10 min.

Apart from surgery, myanesin has been used in a variety of medical states from different spastic conditions in which Buckley Sharp (1947) has achieved some success by oral administration, to tetanus in which Belfrage (1947) has had encouraging results. In one case of tetanus in a boy aged 9 years, the dosage, compared to surgical doses, was enormous; no less than 78 grammes (780 c.c.) in five days. This patient recovered.

A very recent and exceedingly interesting development has been the use of myanesin in veterinary surgery. Mrs. M. Sheppard, M.R.C.V.S., has found it of considerable advantage for abdominal surgery in cats and dogs (1948). Relaxation is obtained with less than half the usual dose of pentothal (the standard anæsthetic technique in this work) with consequent marked improvement in mortality of poor-risk patients.

A number of anæsthetists have commented that myanesin causes respiratory depression. I have not found this to be the case in my own experience; but I have found that the central respiratory depressant effect of pentothal is potentiated by myanesin, and that a short period of apnoea can easily occur when both drugs are given together in the course of an anæsthesia. Potentiation of the one drug by the other was described by Berger and Bradley (1946, 1947) in their work with myanesin on animals. This phenomenon is a *central* depression similar to that produced by pentothal alone and dealt with by intermittent pressure on the rebreathing bag for a minute or two disappears as readily. To the modern anæsthetist then, it is without significance.

It is very different from the dangerous state of *peripheral* respiratory failure with flaccid and toneless thoracic musculature, and loss of resilience and elastic recoil, so disconcertingly like the state of the apparently drowned, which one often experiences as the result of a big dose of curare, and which for reasons I have previously stated here (Mallinson, 1947c) is in my view a frequent cause of serious post-operative morbidity and a major contributing cause of death following the latter drug.

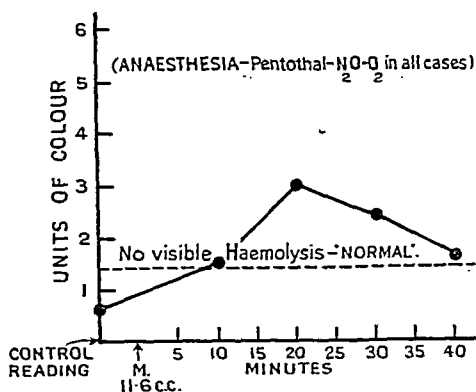
An interesting characteristic of myanesin is that the divergent eyeball sign of first plane anæsthesia is not markedly affected by it, which helps to differentiate between first and second plane anæsthesia when using the curarization technique.

It has been suggested that myanesin causes increased bleeding. No reasons accompany this suggestion in so far as I am aware. This sort of controversy has for years raged round every new anæsthetic introduced, most notably cyclopropane; and in regard to the latter agent still seems far from being settled. One cannot see how the point ever can be settled until a very large series of cases is studied in which all the many variables are controlled in each case—a formidable task. Personally I must record the fact that there have been no complaints about increased bleeding from the surgeons to whose cases I have administered myanesin.

At a meeting of the Section of Anæsthetics held here on April 11, 1947, several speakers reported an alarming series of cases of spreading thrombosis and phlebitis following myanesin. I have found thrombosis of a vein exceedingly uncommon after myanesin both personally and by report, comparable with its incidence after the administration of pentothal; I have never seen phlebitis. I think the answer to this question as regards both drugs is to be found in the technique employed. A fine needle (16–17 gauge hypodermic) *really sharp*, a quick and accurate entry into the vein (all factors which minimize trauma to the vein), and a slow steady injection at about six to eight seconds per c.c. (for the solution is hypertonic) will ensure that the operator is rarely troubled with thrombosis.

In my own experience of some 1,500 myanesin injections I have only once or twice encountered thrombosis of limited degree, not developing into phlebitis, and I have no idea as to whether the lesion occurred at the site of a pentothal or a myanesin injection. I have had several patients come to operation with veins already thrombosed by uroselectan injections, blood transfusions, &c., but these have not developed any further lesions with myanesin. It seems to me in any event that a great deal has been made of a minor complication which is after all, according to Dickson Wright (1948), “annoying rather than dangerous” and is rarely even noticed by the patient.

no definite hæmolysis in this mixture, even after incubation for forty-five minutes, the curve this time showed rupture commencing at 0.65% which was complete at 0.5%. This indicates that myanesin in sufficient concentration (4%) renders the red cells more fragile and therefore that they will hæmolyse more readily when subjected to the trauma of withdrawal through a needle and squirting into a glass vessel. It does *not* indicate that myanesin causes hæmolysis *in vivo*. It suggests that the hæmolysis observed by Pugh and Enderby might have been an artefact. Further experiments by Dr. Gray on the blood of patients receiving myanesin during operation strengthen this suggestion. Samples of blood were withdrawn from a series of 20 patients during anaesthesia, before the administration of myanesin (to serve as a control) and at varying intervals afterwards. A method was devised of estimating the proportion of free hæmogoblin present in the serum of the samples, using King's methyl red standard for bilirubin. No hæmolysis could be observed with the naked eye at readings below 1.4; therefore readings below 1.4 can be taken as clinically normal. To avoid the tedium of considering a whole series of tables from 20 patients with similar readings, the results are averaged here in one graph (Graph I). The highest reading in the



GRAPH I.—Degree of hæmolysis in samples of blood withdrawn after myanesin 10% — average of 20 cases.

whole series was 6.4, the lowest control reading was 0.3. Now if hæmolysis took place in the body on the injection of myanesin it would surely show its maximum effect almost immediately, as the liberated hæmogoblin spread rapidly through the circulation. If on the other hand the effect of myanesin was not to liberate hæmogoblin but to cause increased fragility of the red cells, as is suggested by Dr. Gray's first experiment, one would expect the number of cells rendered more fragile in the samples (and therefore the degree of hæmolysis produced on their withdrawal) to increase slowly, as the damaged cells spread throughout the circulation up to a maximum and then to start falling as these damaged cells were removed from the blood-stream by the reticulo-endothelial system. Such in fact is the case. There is little evidence of any hæmolysis in the sample withdrawn ten minutes after the administration of myanesin. The maximum is reached only after twenty minutes on the average from the time of the injection. At thirty minutes the reading is falling, and at forty minutes it is still falling. In my view therefore the experiments described by Pugh and Enderby to show that hæmolysis is caused *in vivo* by a dose of myanesin injected at a reasonably slow rate (say six to eight seconds per c.c.) into a rapidly moving blood-stream in a vein the calibre of an antecubital vein are fallacious; and their conclusion that myanesin is a dangerous drug to inject is unsubstantiated. Belfrage (1947) records that his tetanus cases (referred to earlier) had no evidence of hæmolysis despite the colossal doses they received. Furthermore I have not myself as yet been able to adduce any sure evidence that the colour in the urine is due to hæmogoblin, with one notable exception. In a third coloured urine obtained since the urine analyses described earlier, iron has been detected by chemical analysis. The proportion was not large, 1.6 mg. in a 250 c.c. specimen, equivalent to 6.4 mg. per litre. The normal content of iron in the urine is given by Hawk, Oser, and Summerson (1947), as varying between 0.7 to 3 mg. per litre, or 1 to 5 mg. daily. This patient had also received, at the same time as the myanesin injected, no less than 20 c.c. of 30% lithocaine into a varicose vein. This substance is a known hæmolysant and according to Foote (1948) should never be employed in doses in excess of 5 c.c.

Whilst the possibility of occasional slight hæmoglobinuria due to a slight degree of late hæmolysis of some of the fragilized red cells cannot at present be excluded (and so far as

TABLE III.—KIDNEY FUNCTION. MYANESIN (22 Cases)

Sex	Age	Operatn. trauma	Time min.	Pre-operative		Post-operative		Day	Myan- esin c.c.	Anæsthetic (Plane I)
				B. urea mg.	U.C.T. %	B. urea mg.	U.C.T. %			
F	33	++	75	25	100	50	47	5th	20	Pentothal N ₂ O—O ₂
F	51	+	75	20	87	20	126	7th	8	Pentothal N ₂ O—O ₂
F	32	+	55	20	101	50	44	5th	10	Pentothal N ₂ O—O ₂
M	59	++	40	48	60	36	120	6th	13	Pentothal N ₂ O—O ₂
M	83	++	70	50	60	52	52	7th	5	Pentothal N ₂ O—O ₂
M	63	—	50	30	122	50	106	8th	6	Pentothal N ₂ O—O ₂
F	20	—	30	40	88	36	68	7th	7	Pentothal N ₂ O—O ₂
F	50	+	35	20	59	20	47	7th	14	Pentothal N ₂ O—O ₂
F	63	—	40	30	68	30	53	7th	10	Pentothal N ₂ O—O ₂
F	36	—	40	20	77	20	66	7th	8	Pentothal N ₂ O—O ₂
F	33	+-	30	30	62	48	59	7th	17	Pentothal N ₂ O—O ₂
M	73	+	60	48	64	40	63	9th	18	Pentothal N ₂ O—O ₂
F	40	+	45	20	103	20	65	5th	20	Pentothal N ₂ O—O ₂
F	38	+-	30	25	154	85	28	5th	20	Pentothal N ₂ O—O ₂
F	35	+-	75	25	81	30	68	7th	10	Pentothal N ₂ O—O ₂
F	33	+	55	20	52	20	53	6th	20	Pentothal N ₂ O—O ₂
F	50	+	40	20	77	45	136	5th	19	Pentothal N ₂ O—O ₂
F	40	++	75	30	47	35	104	5th	10	Pentothal N ₂ O—O ₂
M	72	+	65	40	109	49	68	6th	9	Pentothal N ₂ O—O ₂
F	45	++	45	20	37	40	36	6th	15	Pentothal N ₂ O—O ₂
F	44	—	35	28	109	24	158	5th	10	Pentothal N ₂ O—O ₂
M	36	+-	55	26	50	62	54	7th	25	Pentothal N ₂ O—O ₂
CONTROLS (13 Cases)										
F	50	++	60	40	32	28	49	7th		Pentothal N ₂ O—O ₂
F	42	+	70	20	107	20	52	5th		Pentothal-Spinal
F	32	+-	40	20	101	20	83	5th		Pentothal-N ₂ O-Ether
F	35	+-	40	20	70	20	63	5th		Pentothal-N ₂ O-Ether
F	63	+	70	55	53	35	64	7th		Pentothal-N ₂ O—O ₂
F	62	+++	330	33	152	28	109	5th		Pentothal-N ₂ O-Ether
F	51	+-	20	20	35	25	139	5th		Spinal
F	30	++	70	30	148	45	71	5th		Pentothal-N ₂ O-Spinal
F	44	+	50	30	120	40	55	5th		Pentothal-N ₂ O-Spinal
F	40	+	45	20	55	25	93	5th		Pentothal-N ₂ O-Spinal
F	35	++	70	35	29	20	106	6th		Pentothal-N ₂ O-Trilene
F	37	+++	180	32	92	20	123	7th		Pentothal-N ₂ O-Ether
F	39	+++	180	28	73	44	81	5th		Pentothal-N ₂ O-Ether

U.C.T. = Urea Clearance Test.

except that some deterioration of renal function after operation and anæsthesia appears to be frequent though not invariable, as is well known from the work of Beecher (1938), Hawk, Orth, and Pohle (1941), Darmady (1947*b*), and others, and that this deterioration cannot be definitely related to any particular anæsthetic though it appears to be more marked after spinals and is possibly related to some extent to the degree of trauma.

About this time there appeared a paper by Pugh and Enderby (1947) describing "apparent hæmoglobinuria" following myanesin administration and experiments to demonstrate the occurrence of hæmolysis with myanesin *in vitro*. No details were given as to the methods of handling the blood in these *in vitro* experiments, such as the anticoagulant employed, whether the cells were washed, &c., and no account seems to have been taken of the degree to which these or other factors such as trauma to the red cells on withdrawal through a syringe and needle may have been responsible for the hæmolysis thus demonstrated. Deductions were made from this hæmolysis *in vitro*, postulating a dangerous degree of hæmolysis *in vivo*; supported by one or two isolated experiments in which myanesin (diluted with distilled water, itself a hæmolytic agent) was injected into a wrist vein (almost certainly a vein of small calibre) and at an unknown rate, and blood simultaneously withdrawn from a vein immediately above. These experiments of Pugh and Enderby, however, contained another fallacy, which was demonstrated to me by Dr. Davidson Gray (1947) whose interest and unselfish help I gratefully acknowledge. Dr. Gray plotted a fragility curve with washed red cells from a normal person suspended in normal saline. The curve was within normal limits, no cells rupturing in falling concentrations of NaCl down to 0.45%. This curve was repeated with more of the same cells whose suspension had been made up to contain myanesin in 2% concentration. The mixture was incubated with the cells for forty-five minutes. The fragility curve was the same. The same experiment was again repeated this time using 4% myanesin-saline suspension. Although there was

TABLE IV (310 Cases)

(a) Operation types			(b) Anaesthetic techniques		
Gastric	19	} UPPER ABDOMINAL : 45	Pentothal-N ₂ O-O ₂ ..	33	
Gall-bladder	6		Pentothal-C ₃ H ₈ ..	12	
Miscellan.	20				
Elective	41	} LOWER ABDOMINAL : 237	Pentothal-N ₂ O-O ₂ ..	195	
Emergency	4		Pentothal	12	
Gynaecologic	95		N ₂ O-O ₂	2	
Cæsarean	9		Pentothal-C ₃ H ₈ ..	22	
Prostatect.	29		C ₃ H ₈	1	
Appendicect.	35		Pentothal-Spinal ..	1	
Herniotomy	47		Pentothal-G.O.E. ..	3	
Ac. Obstruct.	2		Gas-oxygen-ether ..	1	
Miscellan.	20				
Elective	226	} PERINEAL : 28	Pentothal-N ₂ O-O ₂ ..	14	
Emergency	11		Pentothal	14	
Rectal	17				
Colpo-Repair	11				

(c) Risk Grouping

	A	B	C	D	1-40	41-60	61-70	71-80	Over 80
Upper abdom. (45)	9	19	16	1	11	23	6	5	—
Lower abdom. (237)	76	122	36	3	114	78	25	16	4
Perineal (28)	15	10	3	0	9	9	6	3	1
Total	100	151	55	4 (310)	134	110	37	24	5

(d) Age Grouping

TABLE V.—POST-OPERATIVE VOMITING

	(1-3 times)	(three +)	Males	Females	Total
Upper abdom (45) ..	4.4%	2.2%	Nil	6.6%	6.6%
Lower abdom (237) ..	12.0%	12.0%	3%	21.0%	24.0%
Perineal (28)	16.6%	Nil	Nil	16.6%	16.6%
Gynaecologic (115) ..	20.0%	14.5%	—	34.5%	—

TABLE VI.—PULMONARY MORBIDITY

In 282 Abdominal Operations

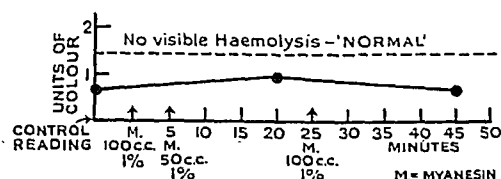
(A) Patients with HEALTHY respiratory systems (154)		(B) Patients with INFECTED respiratory systems (128)		Overall Totals	
<i>Upper (24)</i>		<i>Upper (21)</i> { Major Infectns. 5 Minor Infectns. 16		<i>Upper (45)</i>	
Cough-NPS 4.2%		Cough-NPS 0.9%		Cough-NPS 2.2%	
Bronchitis .. 4.2%		Bronchitis .. 4.8%		Bronchitis .. 4.4%	
Pneumonia Nil		Pneumonia Nil		Pneumonia Nil	
Atelectasis .. Nil		Atelectasis .. 9.6%		Atelectasis .. 4.4%	
Total 8.3%		Total 14.3%		Total 11.0%	
<i>Lower (130)</i>		<i>Lower (107)</i> { Major infectns. 22 Minor infectns. 85		<i>Lower (237)*</i>	
Cough-NPS 3.0%		Cough-NPS 0.9%		Cough-NPS 2.1%	
Bronchitis .. 1.5%		Bronchitis .. 3.7%		Bronchitis .. 2.5%	
Pneumonia Nil		Pneumonia 0.9%		Pneumonia 0.4%	
Atelectasis .. Nil		Atelectasis .. 0.9%		Atelectasis .. 0.4%	
Total 4.5%		Total 6.4%		*Total 5.4%	
<i>Total morbidity</i>		<i>Total morbidity</i>		<i>Total morbidity</i>	
Healthy cases 5.2%		Infected cases 7.9%		Overall .. 6.4%	

* Out of 237 lower abdominal cases 47 hernias produced 14.8% morbidity.

NPS = No Pulmonary Symptoms.

I am aware fewer than 20 cases with apparently hæmoglobinuric urine have so far been reported out of an estimated 10,000 administrations of myanesin) it is known that coloured degradation products of myanesin occur. In addition small quantities of red and brown oily-like substances have been extracted from perfectly normal urines of patients, following myanesin administration, by Hartley and Bradley (1948). This suggests that in some patients, possibly with an inborn variation of metabolism, myanesin like some other chemical substances is capable of colouring the urine. In the majority of patients passing coloured urines then, it seems likely that an explanation on these lines must be sought and the matter needs further investigation. In the minority of cases, if true hæmoglobinuria can be proved, one must consider the possibility that it is due to a few fragilized cells suffering delayed rupture in a patient whose red cell fragility is greater than normal. In the meantime it is clear that these urines, when they do make their rare appearances, need to be examined with the utmost caution before they are labelled hæmoglobinuric.

It can be predicted, however, from our experiments that the slower the rate of injection of myanesin or the smaller the percentage of the drug in the injection the less will be the proportion of fragilized cells circulating. In order to confirm this prediction a further series of cases was studied on the lines of Dr. Gray's second experiment, using 1% myanesin. There was no evidence of hæmolysis in the samples after their withdrawal from the circulation and therefore no increased fragility of red cells produced by 1% myanesin. This chart (Graph II) is typical of the series. The administration of 1% myanesin is simple and trouble-



GRAPH II.—C. H., aged 50. Gastrectomy. Degree of hæmolysis in samples of blood withdrawn after myanesin 1%. Anæsthesia: Pentothal 1.3 g.— N_2O-O_2 —myanesin 1%. Total pentothal: 1.35 g. Total myanesin: 300 c.c. 1%.

free. The apparatus for continuous pentothal described by Macintosh and Pask (1941) has been adapted for the purpose. The screw-topped bottle is graduated in units of 20 c.c. and 100 c.c. up to a half litre. Filled with normal saline it is autoclaved. 50 c.c. of myanesin solution are added before use. Thus each 20 c.c. of the solution is equal to 2 c.c. of myanesin 10%. If all the solution is not used during an operating session the remainder can be re-autoclaved and kept for a subsequent occasion. A larger needle is advisable to get a rapid flow; 1 gramme myanesin can thus be administered in two to three minutes.

I should like to record a series of abdominal and perineal cases illustrating the clinical results of the use of myanesin as a muscle-relaxant. This series consists of 310 cases and is a small one for two reasons. First because it only includes cases in which myanesin has been employed when a relaxing agent was really needed and contains no amputations, orthopædic operations and the like. Secondly it consists only of those cases which could be adequately followed up and excludes many nursing home and other patients where time, distance, or lack of reliable assistance precluded accurate observation. Table IV indicates the types of operation and anæsthetic concerned; the risk distribution is also shown, and by its proportion of B and C grades emphasizes that there has been no bias towards selection of favourable cases.

The same may be said of the age distribution. The age range of myanesin has been from 3 to 90 years. Table V shows the incidence of post-operative vomiting which has been satisfactorily low, when the high proportion of gynæcological cases (generally agreed to have a high vomiting rate according to Russell Davies (1941) and others) is noted. Table VI shows the incidence of post-operative pulmonary complications. The figures are higher than those I published in 1943 and 1944, not only because the age-groups are higher than one's wartime patients, but also because one is now dealing with a civilian population debilitated by a long period of rationing, and in the last two years by an actual and increasing shortage of good food. Here again one type of case, the hernia, well known as having a high morbidity rate, is responsible for a high proportion of the total complications, no less than half its group in fact. Even so the percentages are well below the best of Lucas's series (1944) on chest complications in hernias. It may also be observed that *no complication* of any severity occurred in any patient whose respiratory tract was healthy before operation. This illustrates well the advisability, often stressed but seldom acted upon, of postponing elective operations, whenever possible, till the respiratory tract is satisfactory.

DISCUSSION

To define the present position of myanesin as a therapeutic agent is not easy. It seems to me that we still have a long way to go both with curare and myanesin before a true evaluation of either is possible.

There is no question in my hands of the efficiency of myanesin as a muscle relaxant under light anaesthesia. The papers published and already referred to are in agreement on this point. The summarized opinion of my surgical colleagues is that relaxation with myanesin is as good as with curare. Both drugs have their disadvantages. Some of those associated with curare are formidable. Bronchospasm now seems established as a characteristic reaction of curare according to the work of Landmesser (1947) and although clinically it does not appear to be so common as might be expected, it is an exceedingly dangerous state of affairs when it does occur. Another potentially dangerous characteristic of curare described by many writers including Gross and Cullen (1945), Landmesser (1947), Durrans (1947), Dawkins (1947), and Lyall (1947), is its capacity for producing severe post-operative hypotension. Satisfactory relaxation without complete intercostal paralysis is often difficult to achieve with curare, and not infrequently there is diaphragmatic paralysis as well. These are phenomena to be avoided unless there is a very good and sufficient reason for their toleration. It has been suggested that, *inter alia*, one of curare's greatest disadvantages, largely as a result of the aforementioned characteristics, is the imperative need for its employment to be restricted to the experienced administrator.

All this, however, is not necessarily to condemn the use of curare. Many other anaesthetic agents in common use to-day have astonishing potentialities for causing damage; far greater than those of curare. Much cerebral congestion amongst anaesthetists has been caused by the introduction in myanesin of a drug which possibly causes occasional slight haemoglobinuria, ignoring the fact that a number of drugs employed every day are known haemolysants and producers of haemoglobinuria such as lithocaine, N.A.B. and many others. It might be worth while to recall that Coller and Eastman (1943) showed that cyclopropane anaesthesia was attended by a significant decrease in glomerular filtration rate, and that this phenomenon associated with blood loss or shock could cause sufficient hypotension to result in total renal failure; and not infrequently resulted in renal impairment lasting up to a week. Again, Bastedo (1932) states that patients may occasionally develop nephritis with albuminuria and haematuria after ether anaesthesia, and MacNider (1920) described anuria following ether in 43 out of 131 dogs. Finally Underhill (1948) has shown that even pentothal appears to be capable of marked haemolysis.

With curare the number of deaths so far reported added to the unofficial deaths make up no mean total. Although curare and myanesin are both highly efficient relaxants in light anaesthesia, the hazards of the former (if the number of deaths only is considered) seem to me to be significantly greater than those of the latter. Furthermore, although curare has an undoubted place in the anaesthetist's armamentarium, its dangers and critical dosage circumscribe its general application and restrict its employment only to the highly expert. Myanesin on the other hand has a very wide margin of safety in dosage and 10,000 administrations have brought to light no deaths clearly resulting from its employment and only one significant possible complication. That possible complication, haemoglobinuria, would appear to be rare, and in any event its dangers seem to me to have been perhaps a little exaggerated.

Thus I would suggest from our experience up to date of myanesin that its continued use as a muscle relaxant in anaesthesia is at least as justified as is that of curare; that it can with advantage replace curare for many purposes; and that on balance it has increased the safety of the technique of muscle-relaxation by the method of "curarization".

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Table VII illustrates the efficiency of myanesin in a type of operation where a very high degree of sustained relaxation is essential. The amount of pentothal needed is very small,

TABLE VII
GASTRECTOMIES—12 Cases: *Pentothal-N₂O-O₂: Plane I Anaesthesia*

Age	Sex	Time		Dose pento. grammes	Dose myanesin c.c.	Remarks
Hrs.	min.					
39	M	0	50	0.75	28	—
57	M	2	10	1.55	30	—
54	F	1	45	1.00	13	—
50	M	1	40	1.35	30	—
32	M	1	30	0.75	16	—
48	F	0	50	0.25	17	Very ill, dehydrated. Frail
65	M	1	20	1.05	15	—
38	M	0	50	0.75	25	—
28	M	1	55	1.75	48	Very muscular, sthenic labourer
48	F	1	35	1.00	20	—
46	M	1	40	1.5	24	Very sthenic type
56	F	0	50	0.6	10	—
Average:		1	24	1.02	23	

averaging only 1.12 grammes for an average operation time of seventy-two minutes. The benefit of these minimal amounts of a potent anæsthetic agent is reflected in the improved general state of the patients after operation.

There have been six deaths in this series occurring within seven days of operation, or from complications arising within that period (Table VIII). I think it will be agreed that the

TABLE VIII
Post-operative Deaths: First Seven Days

Age and Sex	Operation	Risk	Condition	Opn. time	Time death	Cause and post-mortem
S. D. 60 yrs. M	Obstructn. carc. cæcum	C.	Cachectic dehydrated distended	2½ hrs.	7th day	Fibrillation, cardiac failure
M. H. 71 yrs. M	Nephrolithotomy giant stone branched	C.	Angina. B.P. 250/110	70 min.	12 hrs.	Shock. Hæmorrhage. Cardiac failure. P.M. arteriosclerosis. Coronary disease myocard. degen. Advanced renal fibrosis.
C. H. 50 yrs. M	Gastrectomy D.U. grossly adherent to pancreas	B.	Hæmatemesis 9 days ago	1¾ hrs.	3rd day	P.M. Leaking duodenal stump, biliary peritonitis
J. W. 65 yrs. M	A.P. resectn. rectum	C.	Op. abandoned. Gross involvement with bladder	2 hrs.	6th day	Ileus and peritonitis
W. J. 40 yrs. F	Panhysterectomy	C.	O.C. nephritis. O.C. rheumatic fever. Very frail; severe shock and hæmorrhage	35 min.	18 hrs.	Pelvis full of blood at P.M. hæmorrhage from L. uterine veins. Recent (pre-op.) cerebral thromb. with spreading cerebral œdema
V. V. 50 yrs. F	Hysterectomy	B.	Operation v. difficult. Shock + +. Obese	2½ hrs.	8th day	At P.M.: Large heart and fatty myocard.; Kidney: post-op. traumatic uræmia syndrome

first five of them are entirely unconnected with the anæsthetic. In the sixth, I personally am satisfied that the syndrome of post-operative traumatic uræmia was sufficient to account for death.

DISCUSSION

To define the present position of myanesin as a therapeutic agent is not easy. It seems to me that we still have a long way to go both with curare and myanesin before a true evaluation of either is possible.

There is no question in my hands of the efficiency of myanesin as a muscle relaxant under light anaesthesia. The papers published and already referred to are in agreement on this point. The summarized opinion of my surgical colleagues is that relaxation with myanesin is as good as with curare. Both drugs have their disadvantages. Some of those associated with curare are formidable. Bronchospasm now seems established as a characteristic reaction of curare according to the work of Landmesser (1947) and although clinically it does not appear to be so common as might be expected, it is an exceedingly dangerous state of affairs when it does occur. Another potentially dangerous characteristic of curare described by many writers including Gross and Cullen (1945), Landmesser (1947), Durrans (1947), Dawkins (1947), and Lyall (1947), is its capacity for producing severe post-operative hypotension. Satisfactory relaxation without complete intercostal paralysis is often difficult to achieve with curare, and not infrequently there is diaphragmatic paralysis as well. These are phenomena to be avoided unless there is a very good and sufficient reason for their toleration. It has been suggested that, *inter alia*, one of curare's greatest disadvantages, largely as a result of the aforementioned characteristics, is the imperative need for its employment to be restricted to the experienced administrator.

All this, however, is not necessarily to condemn the use of curare. Many other anaesthetic agents in common use to-day have astonishing potentialities for causing damage; far greater than those of curare. Much cerebral congestion amongst anaesthetists has been caused by the introduction in myanesin of a drug which possibly causes occasional slight haemoglobinuria, ignoring the fact that a number of drugs employed every day are known haemolysants and producers of haemoglobinuria such as lithocaine, N.A.B. and many others. It might be worth while to recall that Coller and Eastman (1943) showed that cyclopropane anaesthesia was attended by a significant decrease in glomerular filtration rate, and that this phenomenon associated with blood loss or shock could cause sufficient hypotension to result in total renal failure; and not infrequently resulted in renal impairment lasting up to a week. Again, Bastedo (1932) states that patients may occasionally develop nephritis with albuminuria and haematuria after ether anaesthesia, and MacNider (1920) described anuria following ether in 43 out of 131 dogs. Finally Underhill (1948) has shown that even pentothal appears to be capable of marked haemolysis.

With curare the number of deaths so far reported added to the unofficial deaths make up no mean total. Although curare and myanesin are both highly efficient relaxants in light anaesthesia, the hazards of the former (if the number of deaths only is considered) seem to me to be significantly greater than those of the latter. Furthermore, although curare has an undoubted place in the anaesthetist's armamentarium, its dangers and critical dosage circumscribe its general application and restrict its employment only to the highly expert. Myanesin on the other hand has a very wide margin of safety in dosage and 10,000 administrations have brought to light no deaths clearly resulting from its employment and only one significant possible complication. That possible complication, haemoglobinuria, would appear to be rare, and in any event its dangers seem to me to have been perhaps a little exaggerated.

Thus I would suggest from our experience up to date of myanesin that its continued use as a muscle relaxant in anaesthesia is at least as justified as is that of curare; that it can with advantage replace curare for many purposes; and that on balance it has increased the safety of the technique of muscle-relaxation by the method of "curarization".

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Dr. G. E. Hale Enderby: Dr. Mallinson has tried to persuade us that the hæmolysis occurring with myanesin does not matter. He also apparently goes so far as to doubt whether hæmoglobinuria does occur, and whether the work which Dr. Pugh and I did on this subject is, in fact, correct. In answer I must refer Dr. Mallinson to our publication (Pugh, T. J., and Enderby, G. E. Hale, 1947, *Lancet* (ii), 387), where all the details of our experiments are given, which show conclusively that hæmolysis occurs in the blood-stream, and hæmoglobin has been found in the urine of three cases.

Mention was made of hæmolysis following such commonplace injections as pentothal, and I must agree that it does occur to a very small extent with this drug. However, it is obvious that the degree of hæmolysis is the important factor, and with myanesin the hæmolysis is immediate and extensive, accompanied by an alarming protein precipitation. Those who still use this drug must have observed the immediate lysis occurring in the syringe following aspiration of blood, and how different this is with pentothal, where half an hour may show little change. I personally know three anæsthetists who will not use this drug again, for they consider it very dangerous.

I would repeat the suggestion I originally made to British Drug Houses that they investigate whether it is the drug itself or the solvent which is producing these undesirable effects. It appears to me that the solvent may be the cause, for it is made up of many chemicals (which I call "anti-freeze"), and furthermore the oral myanesin which has no solvent does not apparently produce these effects.

I must thank Dr. Mallinson for his courage in presenting the details of the fatal cases which he has had. He ascribes death in two of them to traumatic uræmia, which facile explanation I personally cannot accept, particularly in view of the case reported by Hewer and Woolmer (1947, *Lancet* (ii), 909). I consider these cases have a direct relationship with the observed phenomena of hæmolysis and protein precipitation.

Dr. Mallinson mentions the boy with tetanus who received large doses of myanesin. Is it not true that this case developed a complete anuria, but eventually recovered?

Dr. T. Cecil Gray expressed gratitude to Dr. Mallinson for his interesting paper and for giving the Section the opportunity to discuss this dangerous substance, and went on to state that he had had experience of only a small series of cases anæsthetized with the help

of myanesin. The series was small because it very soon became apparent both to himself and the surgeons that in reasonable dosage this substance was ineffective in adults and potentially dangerous.

It was ineffective because in a light plane of anæsthesia it did not give good relaxation. The purpose of a relaxant drug should be to give good operating conditions using only minimal amounts of toxic anæsthetic agents. This myanesin did not do. In regard to its potentiation of the barbiturates it was his experience that this substance did not in any way enhance their analgesic powers and the potentiation was only evidenced by a longer time of narcosis post-operatively which was undesirable.

Myanesin was potentially dangerous because of its hæmolytic properties about which a great deal had already been said, and although Dr. Mallinson stated that many drugs have hæmolytic properties the fact remained that there was yet to be reported a case dying from renal failure due to hæmoglobinuria following the use of thiopentone or of any other anæsthetic agent. In Dr. Mallinson's series it was said that the hysterectomy case had died as a result of traumatic uræmia. Surely this complication following hysterectomy must be very rare indeed, and it would seem more reasonable to attribute the uræmia to the known properties of this new agent.

Moreover, myanesin was dangerous because of the incidence of thrombosis which followed its use and he had had one very severe case of this complication. This occurred in a man of 62 undergoing a gastrectomy for carcinoma who received 1.2 grammes of thiopentone and 40 ml. of myanesin. As could be seen from the slide [shown] the forearm and hand on the evening of the operation were grossly œdematous and violently discoloured. Every vein right up to the axilla was thrombosed. In this case there was no question of intra-arterial injection for the injections were given through an intravenous drip and the arterial side of the circulation was undamaged. It was only by the greatest good fortune that the arm recovered.

Dr. Mallinson would doubtless point out that this might be attributable to the thiopentone, but which of those present with all their collective experience had ever seen such a picture following the use of thiopentone administered through large or small needles by rapid or slow injection.

Dr. Mallinson said that myanesin had proved of great use in veterinary surgery; it might be better if the ampoules of this substance were labelled "For use in veterinary surgery only".

Dr. A. J. H. Hewer: Two experiments were performed on cats in which 25 mg. of myanesin per kilogram body-weight were given in a 1% solution at a standard rate.

In the first cat experiment the solution was prepared by diluting the 10% solution supplied by the makers down to 1% with normal saline.

In the second experiment, a 1% solution of myanesin powder was made in normal saline. Blood taken from the first cat five minutes after injection showed more hæmolysis than that taken from the second. This suggests that the solvent is capable of causing hæmolysis as well as myanesin itself.

Dr. A. R. Hunter said that Miss Waterfall and he had been able to do some work on myanesin at the Manchester Neurosurgical Unit.

Their interest in the possibilities of the use of myanesin in hyperkinetic states was aroused when he had had the misfortune to produce, by the injection of 30 c.c. of myanesin (a dose which was entirely necessary to produce adequate muscular relaxation in the patient concerned), a simultaneous failure of circulation and respiration which was almost certainly of central origin. This was at once reversed by the intravenous injection of 5 c.c. of nikethamide, which, in addition, abolished the muscular relaxation. Since most analeptic drugs were also convulsants, acting centrally on the brain, he decided to try the effect of myanesin in various hyperkinetic states. Miss Waterfall and he had given the drug on several occasions to patients in status epilepticus, and found that the convulsions ceased almost immediately after its injection. Further, the time which elapsed between the injection of the drug and the cessation of the fits was exactly the same as that which had elapsed on previous occasions, when thiopentone or hexobarbitone had been given for the same purpose. Myanesin was also given to a woman with Parkinsonism, and her movements ceased, but the dosage necessary in her case was about three times that required to make epileptiform convulsions stop. Respective figures were 26 mg. per kilo, and 8 mg. per kilo. Dr. Stephen, of the Montreal Neurological Institute, has also given myanesin to patients with Parkinsonian tremors, and found a like dosage necessary to arrest the movements. He also noted that the drug relieved thalamic pain. He was able too to do electro-encephalograms on his patients and found that myanesin had no effect on the cortical action potentials. In addition he carried out, with Dr. Chandy, a series of observations on

the action currents of muscle and nerve after direct and reflex stimulation under myanesin, and was able to show that the drug had no effect on these phases of neuromuscular activity. It therefore seemed, on the evidence available, that myanesin acted mainly on that part of the brain which gave rise to epileptic activity, and to a lesser extent on the portion which caused the movements of Parkinsonism. The time required between its injection and the appearance of its action was the same as that required for other drugs acting on the cerebrum. It was therefore reasonable to conclude that myanesin affected mainly the motor apparatus of the basal ganglia.

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Dr. Ronald Woolmer said that he would like to associate himself with the remarks of Dr. Cecil Gray. He had found the muscle-relaxing effect of myanesin disappointing. Large doses had to be given to produce satisfactory relaxation, and even then the effect was fleeting and uncertain.

Dr. H. W. Loftus Dale had records of 150 cases, 148 before hæmolysis report and two after; one of the latter developed methæmoglobinuria (Report from laboratory).

The operations in which myanesin had been used were lower abdominals, appendices, suprapubic cystotomies, prostatectomies, oophorectomies and myomectomies. The action was found to be unreliable; relaxation might be good in one case and in a similar case poor or absent, or good until the surgeon produced some stimulus, such as pulling on a mesentery, when the abdomen would close on his wrist like a rat trap.

Since the results which anæsthetists were obtaining with curare were eminently satisfactory from every angle, the surgeons were unwilling to risk myanesin on an upper abdominal operation, hence none were included in this series.

Relaxation of skeletal muscles and abdominal muscles in the absence of stimulation of the peritoneum was found to be good, hence some use was made of myanesin in gynæcology, good relaxation obtained for examinations under anæsthesia and it was a help in getting the patients into the lithotomy position, less thiopentone being required.

In obstetrics, in one case of external version, there was complete failure to get any relaxation which was finally obtained by the use of no less ether than had this agent been used by itself. Dr. Loftus Dale himself did not see this case which had been handled by a competent resident anæsthetist.

In orthopædics myanesin had been used in three cases of manipulation of the spine; the surgeon had put the patients through the most amazing contortions with great ease and facility with the addition of 0.5 gramme thiopentone.

In six cases of major fractures in muscular males, reduction had been effected with great ease under minimal amounts of thiopentone. One unusual case was that of a bull-necked heavily built man with trismus due to a quinsy; 1 gramme of myanesin and a little general analgesia with trilene enabled his mouth to be opened and the situation dealt with in a most satisfactory manner both as regards safety and comfort.

Complications: There were three deaths in the series, none of which was associated with anæsthesia. There were three post-operative "chests", two following male herniorrhaphies and one termination of pregnancy and sterilization in an insane female. In this last case the very large amount of sedatives required both pre- and post-operatively would appear to be the cause.

There were three cases of venous thrombosis, two minor and one very extensive.

The number of cases in this series is too small to justify any conclusions, but, when added to the findings of other workers, may be of some value in assessing the merits or demerits of the substance in question.

Dr. O. P. Dinnick: Myanesin was used for a short series of abdominal cases as a supplement to thiopentone and N_2O-O_2 anæsthesia. The use of the drug was abandoned before the series was completed for the following reasons: (1) The relaxant effect was not nearly so pronounced as that produced by curare or by an intercostal block, and the surgeons commented adversely. (2) The post-operative stupor or sleep was prolonged. (3) There was obvious damage to veins.

In one case thrombosis developed during the operation and spread within half an hour from the site of injection in the forearm up to the shoulder. Next day there was marked inflammation along the infected vein—there was, however, no retrograde or collateral spread of the thrombus. The patient recovered without evidence of emboli.

In two other cases the veins for several inches proximal to the injection site developed a "stickiness" of the intima, and became like perished rubber tubing. In one of these cases the condition was followed by a thrombosis.

In all these cases only myanesin had been injected into the affected veins. The pentothal was injected into adjacent veins which developed no immediate or post-operative thrombosis.

There was one post-operative death in this series—in a trained athlete aged 26 with a carcinoma of the rectum. At laparotomy, when 30 c.c. of myanesin failed to give really satisfactory relaxation, the growth was found to be inoperable and a left iliac colostomy was performed. The condition of the patient next morning was satisfactory, but he died five days later with a blood urea of 350 mg. %. Post-mortem examination was refused. Pugh and Enderby's paper (1947) had not then been published, but his urine was not reported as being discoloured.

Dr. Dinnick hesitated to present this case with so little pathological evidence, and hesitated even more to draw any conclusions. He would only say that their clinical impression—like that of Hewer and Woolmer (1947)—was that this death was unexpected and that the myanesin could not be exempted from suspicion.

It would appear that there were definite risks inherent in the administration of myanesin, and he would say that this drug, in the form at present supplied, had no place in clinical anaesthesia.

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Dr. H. Bruce Wilson said he had initiated an investigation at the Royal Aberdeen Hospital for Sick Children into the properties of myanesin primarily to determine if the drug were effective, and secondly, did it harm the patient? To determine the first, they took a series of children suffering from acute appendicitis, gave them identical premedication, induced anaesthesia with nitrous oxide, oxygen and ether, intubated them with a tube lubricated with nupercaine paste, and then lightened the anaesthesia to Plane 1. At this stage as would be expected, relaxation of the abdominal muscles was not present, but on the surgeon reaching peritoneum, a dose of myanesin was injected, and in all cases except 3, in a series of 60, adequate relaxation was obtained. In those cases where relaxation was not obtained, the anaesthesia was deepened, and the important finding was that relaxation was achieved at a lighter plane of anaesthesia than if myanesin had not been used. This satisfied them that myanesin had the power of lowering the tone of the abdominal muscles and allowing the surgeon adequate conditions for operating. He would emphasize that the relaxation obtained with myanesin was not to be compared with the extreme relaxation which one obtained when using *d*-tubocurarine chloride, but he felt it to be an honest clinical finding that there was lowered tone of the abdominal muscles when myanesin was used.

To determine if the drug had any harmful effect, they charted all cases on Nosworthy Cards, did routine pre- and post-operative urinary examinations, and, in addition, routine urea clearance tests. All these proved negative. It was only after Pugh and Enderby's report of haemoglobinuria that they carried out spectroscopic tests of the urine (these were negative) and examination of the blood before induction of anaesthesia, once anaesthesia was established, and after myanesin had been injected. They found that in every case where myanesin was introduced into the blood-stream, some degree of intravascular haemolysis occurred, along with a definite increase in the fragility of the red blood cells. As the patients showed no clinical ill-effect and no abnormal urinary constituents were discovered, they felt justified in proceeding with the investigation. Since the publication of their initial report, they had had two cases of haemoglobinuria but with no apparent ill-effect. They felt that the solvent and not the myanesin itself was the agent responsible for the haemolysis. Colleagues had been using oral myanesin in orthopaedics and had had no ill-effect. Further investigation into the question of haemolysis was required before one could confidently employ myanesin.

Dr. F. Barnett Mallinson in reply: Dr. Enderby will remember that in the text of the paper I have just read, I was careful to avoid stating that myanesin does not cause haemoglobinuria; only that I had not, as yet, any certain evidence of it.

I think Dr. Underhill has demonstrated conclusively that *in vitro* experiments cannot be applied to this problem—otherwise we must stop using thiopentone, a strong haemolytic *in vitro*.

With regard to Belfrage's case of tetanus: the boy did not develop anuria. A severe drop in urine output was recorded (not a surprising thing in a patient so gravely ill).

Myanesin was stopped following laboratory findings on the blood urea the figures of which were afterwards found to have been erroneously reported.

Dr. Gray starts off by referring to "this dangerous substance" even before he attempts to show that, in fact, it is so; thus one is immediately led to suspect a biased approach. Dr. Gray then tells us that myanesin is ineffective, but admits that he has only used it in a few cases. Regarding these points then he answers himself. I can only suggest to him a perusal of the half-dozen papers I have just quoted in which the authors' careful study of the drug is manifested by the properly recorded series of cases with which they support their favourable opinion.

I should like to pay tribute to Dr. Gray's work on curare which shows very properly his enthusiasm for this substance, following the recent use of which the reported (and unreported) deaths have already caused a considerable number of anæsthetists to express no little anxiety concerning it. Personally I still adhere to the opinions expressed on curare in my preliminary report of its first use in this country (1945, *Lancet* (ii), 75), but still use it, because I am aware of the dangers inherent in any potent drug if mishandled. Myanesin after some 10,000 administrations has yet to show a death clearly due to its employment. Regarding the hysterectomy upon which Dr. Gray comments, I incline to the diagnosis of an acknowledged expert expressed after examination of an actual pathological section.

Dr. Gray shows a slide of an arm whose condition he says supervened following myanesin injection. He now admits that this slide was an artist's impression. I have studied the work of Picasso, Matisse and Chagall and am forced to the conclusion that art is not as scientific a medium as photography for recording facts. In this case Dr. Gray tells us that the myanesin injections were made through an intravenous drip. Not so long ago I unsuspectingly made a number of injections of pentothal into an I.V. drip exceedingly neatly set-up (and bandaged up) in the ward before operation, which was quietly leaking into the tissues all the time. A considerable percentage of the blood and pentothal thus given diffused out into the tissues and produced an arm exactly like this slide. No myanesin had been given.

I have not suggested that any deaths have followed pentothal; but such deaths have been known to occur following various hæmolytic drugs in use clinically.

Dr. Hunter: I would like to thank Dr. Hunter for his contribution to the discussion, from which I have learnt much that interests me. I have used myanesin in Parkinsonism and can confirm his findings.

Dr. Loftus Dale has given us an account of the phenomena which were apparently produced by the injection of myanesin into 150 patients. Many of these appear to have been the very types I pointed out in my paper as having been omitted from my series because there was no point in giving them the drug; cases such as examination under anaesthesia, dilatation and curettage, and orthopaedic operations.

Section of Physical Medicine

President—W. S. TEGNER, M.R.C.P.

[May 22, 1948]

MEETING HELD AT THE ROYAL NATIONAL HOSPITAL FOR
RHEUMATIC DISEASES, BATH

Amyloid Disease and Rheumatoid Arthritis. [Abridged]

By L. C. HILL, M.D., F.R.C.P.

My apology for introducing this subject to-day rests upon my having a patient apparently suffering from this disease at present in one of my beds at the Rheumatic Hospital. The association is so rare that every authentic or even suspected case is of interest. In most of the cases hitherto published amyloidosis has occurred in children with Still's disease. The association with adult rheumatoid arthritis was first noted in 1903, almost simultaneously by Whitman and Spitzzy. Little further was heard of it until 1927 when Carrol and Nelson published a case. Since then, well under 40 cases have been described. It is not sufficiently realized that the fibrinoid degeneration of acute rheumatic infection can continue to the stage of amyloid degeneration (Mervyn Gordon, 1948). Beattie (1906) described four instances of this in pure rheumatism.

It is perhaps permissible to mention briefly some of the features of amyloid disease, and to begin by quoting Hadfield's definition of amyloid as a "structureless, glyco-protein found in the tissues as an insoluble gel and first appearing between the scanty cells of the endothelial lining of capillary blood-vessels". From the pathological point of view it occurs outside the cells and ultimately results in great thickening of the blood-vessel walls. It is steadily progressive and leads to great enlargement and translucency of the affected organs. There are three types:

(1) Primary mesodermal type is rare and arises independently of protein loss or chronic infection. May form large tumour-like masses in larynx, tongue, lymph glands, &c.

(2) In association with multiple myelomatosis with Bence-Jones proteinuria. It is here probably associated with rise in plasma globulin.

(3) Secondary or common type occurs as a complication of long-continued infection, with gross loss of body protein. It affects the capillaries and small vessels of those organs rich in reticulo-endothelium.

The secondary type has been described in a large variety of apparently unrelated processes, all of which have had in common tissue destruction and usually chronic suppuration, but of late secondary type cases have been largely confined to institutions dealing with advanced pulmonary tuberculosis. Recent statistics show it to be present in 40% of all cases of pulmonary tuberculosis which come to post-mortem, and of those diagnosed clinically, approximately 60% are dead within six months. Unfortunately, it is still only recognized clinically in about 25% of cases ultimately proved at post-mortem, which is a pity in view of the fact that radical surgery at an early stage may lead to its retrogression. Whenever in a chronic disease process, a significant fall in the albumin content of the plasma occurs, together with an absolute or relative increase in the globulin, amyloidosis should be suspected. Involvement of the kidneys is serious and the clinical picture produced is usually that of nephrosis. Urea retention or hypertension are very rarely found and in spite of considerable albuminuria, oedema occurs late. It is probably the only manifestation of amyloidosis which can be a direct cause of death. It always alters the prognosis in any disease by increasing the loss of plasma proteins, especially the albumin, via the urine. The urine is usually pale, of consistently low specific gravity, containing a considerable quantity of albumin, and hyaline casts, which of course do not, as was originally taught, contain amyloid. Occasional granular casts are also present.

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I should like to pay tribute to Dr. Gray's work on curare which shows very properly his enthusiasm for this substance, following the recent use of which the reported (and unreported) deaths have already caused a considerable number of anaesthetists to express no little anxiety concerning it. Personally I still adhere to the opinions expressed on curare in my preliminary report of its first use in this country (1945, *Lancet* (ii), 75), but still use it, because I am aware of the dangers inherent in any potent drug if mishandled. Myanesin after some 10,000 administrations has yet to show a death clearly due to its employment. Regarding the hysterectomy upon which Dr. Gray comments, I incline to the diagnosis of an acknowledged expert expressed after examination of an actual pathological section.

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Section of Physical Medicine

President—W. S. TEGNER, M.R.C.P.

[May 22, 1948]

MEETING HELD AT THE ROYAL NATIONAL HOSPITAL FOR
RHEUMATIC DISEASES, BATH

Amyloid Disease and Rheumatoid Arthritis. [*Abridged*]

By L. C. HILL, M.D., F.R.C.P.

My apologia for introducing this subject to-day rests upon my having a patient apparently suffering from this disease at present in one of my beds at the Rheumatic Hospital. The association is so rare that every authentic or even suspected case is of interest. In most of the cases hitherto published amyloidosis has occurred in children with Still's disease. The association with adult rheumatoid arthritis was first noted in 1903, almost simultaneously by Whitman and Spitzzy. Little further was heard of it until 1927 when Carrol and Nelson published a case. Since then, well under 40 cases have been described. It is not sufficiently realized that the fibrinoid degeneration of acute rheumatic infection can continue to the stage of amyloid degeneration (Mervyn Gordon, 1948). Beattie (1906) described four instances of this in pure rheumatism.

It is perhaps permissible to mention briefly some of the features of amyloid disease, and to begin by quoting Hadfield's definition of amyloid as a "structureless, glyco-protein found in the tissues as an insoluble gel and first appearing between the scanty cells of the endothelial lining of capillary blood-vessels". From the pathological point of view it occurs outside the cells and ultimately results in great thickening of the blood-vessel walls. It is steadily progressive and leads to great enlargement and translucency of the affected organs. There are three types:

(1) Primary mesodermal type is rare and arises independently of protein loss or chronic infection. May form large tumour-like masses in larynx, tongue, lymph glands, &c.

(2) In association with multiple myelomatosis with Bence-Jones proteinuria. It is here probably associated with rise in plasma globulin.

(3) Secondary or common type occurs as a complication of long-continued infection, with gross loss of body protein. It affects the capillaries and small vessels of those organs rich in reticulo-endothelium.

The secondary type has been described in a large variety of apparently unrelated processes, all of which have had in common tissue destruction and usually chronic suppurative, but of late secondary type cases have been largely confined to institutions dealing with advanced pulmonary tuberculosis. Recent statistics show it to be present in 40% of all cases of pulmonary tuberculosis which come to post-mortem, and of those diagnosed clinically, approximately 60% are dead within six months. Unfortunately, it is still only recognized clinically in about 25% of cases ultimately proved at post-mortem, which is a pity in view of the fact that radical surgery at an early stage may lead to its retrogression. Whenever in a chronic disease process, a significant fall in the albumin content of the plasma occurs, together with an absolute or relative increase in the globulin, amyloidosis should be suspected. Involvement of the kidneys is serious and the clinical picture produced is usually that of nephrosis. Urea retention or hypertension are very rarely found and in spite of considerable albuminuria, oedema occurs late. It is probably the only manifestation of amyloidosis which can be a direct cause of death. It always alters the prognosis in any disease by increasing the loss of plasma proteins, especially the albumin, via the urine. The urine is usually pale, of consistently low specific gravity, containing a considerable quantity of albumin, and hyaline casts, which of course do not, as was originally taught, contain amyloid. Occasional granular casts are also present.

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The biuret method has been used for the estimation of the plasma proteins and this and the other estimations have been made by Dr. H. J. Gibson and his staff by routine methods in his laboratory. We are grateful to him for this service and also for his personal help and advice over the whole problem.

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I shall describe the results of plasma protein estimations obtained initially in 24 cases of rheumatoid arthritis, and 5 cases of ankylosing spondylitis, and the effects of blood transfusions on 21 cases of rheumatoid arthritis which we have followed up for at least one month.

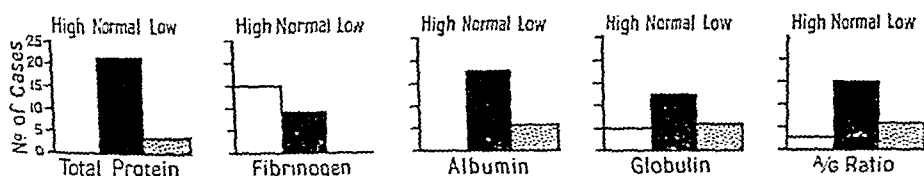


FIG. 1.—Initial plasma protein figures in 24 cases of rheumatoid arthritis.

Analysis of initial findings of 24 cases of rheumatoid arthritis.—The chart (Fig. 1) is divided into three columns reading from left to right: high values, normal values, low values. The number of cases is represented on the ordinate. It will be seen that 21 cases of rheumatoid arthritis show normal total protein figures and 3 cases show slightly low figures. Fibrinogen readings are high in 15 cases and normal in 9. Where normal they were at the upper limit of normality (0·35–0·4 gramme %). Albumin was normal in 18 cases, in 6 it was low and in these cases it was associated with a raised globulin in every case but one. The globulin shows a normal figure in 13 cases, a high figure in 5 cases and a low figure in 6 cases. The A/G ratio shows a normal figure in 15 cases, a high figure in 3 cases (in every case due to a low globulin), and a low figure in 6 cases, the latter being due to a raised globulin and an associated low albumin.

Analysis of initial findings in ankylosing spondylitis.—5 cases only were examined. The total protein was high in 3 cases (9·0 grammes % in each case), and within normal limits in 2 cases. Fibrinogen values were high in all cases. Albumin readings were normal in all cases. Globulin was high in 2 cases and normal in 3 cases and the A/G ratio was normal in every case.

The abnormal readings in rheumatoid arthritis were associated with extensive involvement and marked activity as judged from the clinical evidence, from the degree of anaemia, and from the sedimentation rate. The cases showing initial normal readings tended to be either more chronic or very early types. This does not include the fibrinogen figures which tended to be high in all cases.

The most recent method of diagnosis depends upon the capacity of amyloid tissue to combine with or absorb certain substances in solution in the blood plasma, notably congo red. This rapid absorption of congo red from the plasma is the basis of the Paunz test. In it the dye is injected in the proportion of 1.5 mg. per kg. of body-weight, and samples of the blood are taken at the end of one, two and three hours. If all traces of the dye have disappeared in one hour the result can be considered strongly positive, if at the end of two hours it is highly suspicious.

F. C., aged 37. A gardener.

CASE HISTORY

Admitted to hospital complaining of extensive rheumatoid involvement of joints (28.11.46).

Past history.—Psoriasis and deafness since infancy. Onset of rheumatoid arthritis 1943. Three blood transfusions in 1945, and a course of gold (myocrisin). No improvement.

Family history.—One sister also with psoriasis developed rheumatoid arthritis in 1943, was treated in this hospital on several occasions without apparent benefit, and died aged 44, in December 1947, with a diagnosis of amyloidosis which does not appear to have been confirmed at autopsy.

On examination.—Extensive rheumatoid arthritis with severe generalized muscular wasting, and fibrillary tremors, psoriasis and complete deafness (otosclerosis). X-rays: Typical rheumatoid arthritis appearances.

Blood: Severe microcytic anaemia; Hb 65% = 9.5 grammes. Haematocrit 38%. C.S.R. 56%, plasma uric acid 6.3 mg.%. Berger 2 negative. Blood urea 20 mg.%.
Urine: N.A.D. Urea clearance (Van Slyke) = 184.3% normal.

Treatment.—Physiotherapy, baths, rest, plasters, vitamins, iron, &c., chrysarobin. No improvement.

Readmitted (13.9.47).—Blood: As before, Hb 73%. Blood cholesterol 161 mg.%. Plasma proteins (30.10.47): Total 5.0; fib. 1.05; albumin 1.2, globulin 2.75 grammes %. Ratio, A : G = 1 : 2.

Paunz Test positive. Complete clearance of dye in one hour.

Treatment.—Rest, mild physiotherapy, high protein diet, casydrol. No improvement.

Readmitted (3.2.48).—Steady deterioration. Oedema now generalized. Spleen palpable.

Treatment.—Transfused with 300 c.c. of concentrated plasma, with no improvement in oedema, but plasma protein ratio returned to a more normal level. Total 5.0; fib. 0.7, albumin 3.6, globulin 0.7, Ratio, A : G = 5 : 1. It was not until he was put on to urea in doses of 30 grains t.d.s. that his oedema diminished. The diuretic effect was immediate. General condition improved.

From a study of the literature it seems that when the association occurs the rheumatoid infection is always progressive and intractable and is usually associated with an unusually severe anaemia and emaciation. In most of the recent cases, at least one course of gold and usually more have been given. In the few cases examined alteration in the plasma protein ratio was noted, with a lowering in the albumin level and a relative or absolute rise in the globulin. Renal involvement is always present, and in most cases death can be attributed directly or indirectly to this. The picture is that of the nephrotic kidney, with no evidence of urea-retention or hypertension to the end.

SUMMARY OF INTERESTING FEATURES IN THE ABOVE CASE

- (1) The occurrence in a brother and sister of psoriasis and rheumatoid arthritis is reported. In each case the former began in infancy and the latter in 1943.
- (2) In each a severe hypochromic anaemia was present throughout, and measures to deal with it were relatively unsuccessful.
- (3) The rheumatoid infection was acute in the onset, progressed rapidly and failed to respond to treatment. Gold was given (two courses to the brother, four courses to the sister) without apparent benefit.
- (4) The diagnosis of amyloidosis was suggested in both patients and supported in the brother by a strongly positive Paunz test.
- (5) The nephrotic state in which this patient now is, and from which his sister apparently died, was associated with a violent alteration in the albumin : globulin ratio. Whereas this was corrected by intravenous concentrated plasma, oedema was unaffected and the patient's general condition showed no obvious improvement. Urea and later ammonium chloride, produced an immediate diuresis with all-round improvement.

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Effect of Blood Transfusion on Rheumatoid Arthritis

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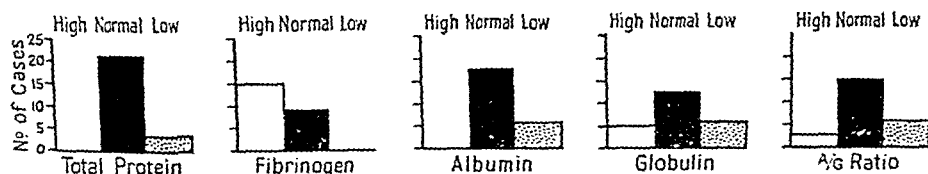


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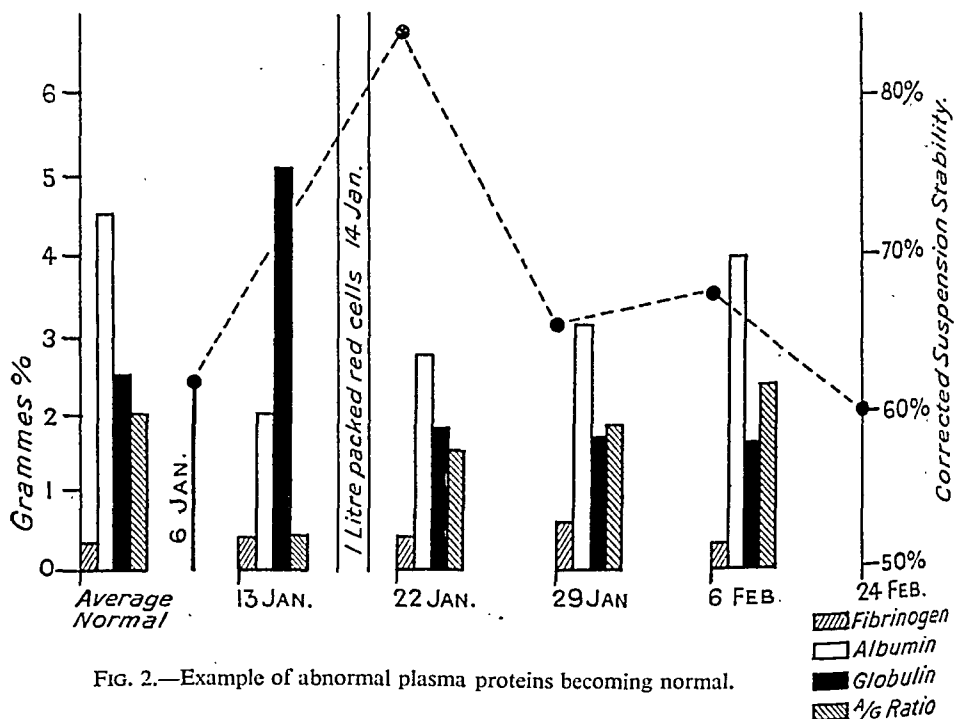


FIG. 2.—Example of abnormal plasma proteins becoming normal.

Effect of blood transfusions on 21 cases of rheumatoid arthritis.—We found that we could divide the cases into three types.

Type 1: 11 cases which showed abnormal protein values initially became normal after transfusion, packed cells being given in every case but one. This case was given whole blood and it also showed a return of normal protein values after transfusion. One of these cases showed a return of abnormal values within a month after transfusion, but not within fourteen days. The other 10 maintained the normal values for at least a month during which time they were observed. Fig. 2 illustrates one case.

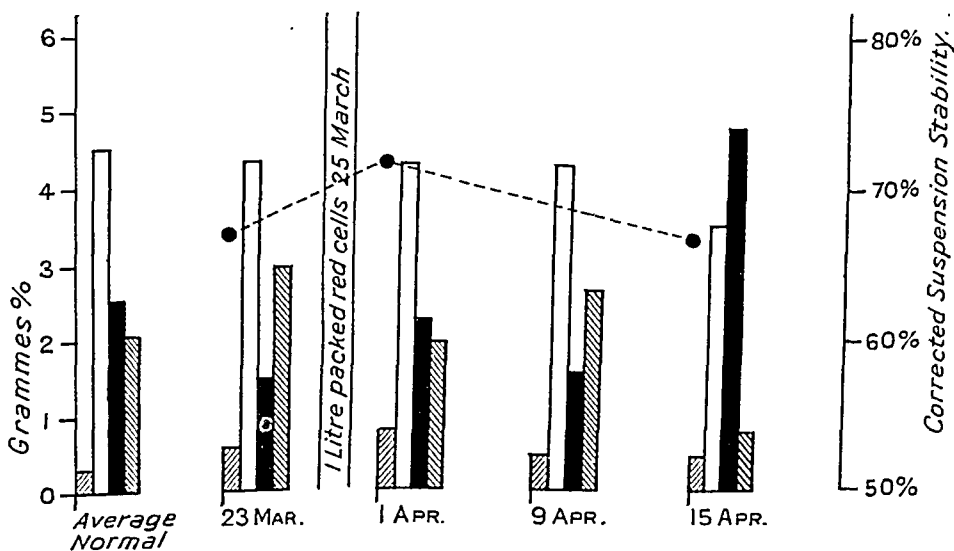


FIG. 3.—Example of normal plasma proteins becoming abnormal.

The dotted line represents corrected suspension stability readings and it will be noted that these show a temporary improvement accompanying the reversal of the abnormal plasma protein values.

Type 2: 5 cases which were normal before transfusion showed abnormal readings during the month after transfusion, but in each case an interval of fourteen days had elapsed before this occurred (see Fig 3). In one case later readings showed a return to normal again.

Type 3: 3 cases which had normal plasma protein readings before transfusion showed no change afterwards (Fig. 4).

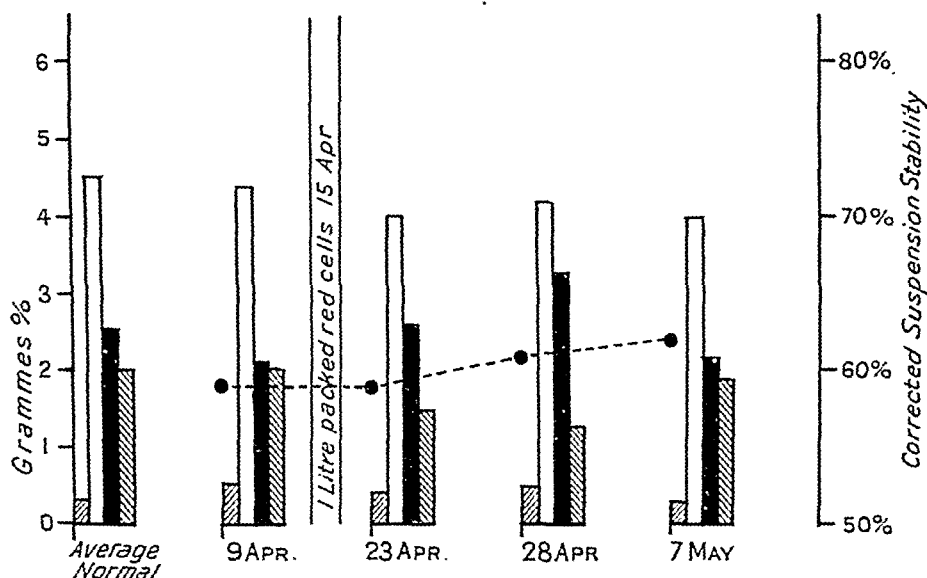


FIG. 4.—Example of normal plasma proteins staying normal.

Two cases which were transfused with plasma alone had normal figures before transfusion, and continued to show normal figures afterwards.

We intend to find the effect of plasma on cases showing initial abnormal plasma proteins as soon as possible.

So far we do not find it easy to correlate these changes with other changes found in the blood. We find that the return to normal values is coincident with a betterment in the general condition of the patient. We do not think that there is any immediate objective improvement in the articular condition but this is very difficult to assess.

Dr. D. Hall Brooks : Dr. Simpson has mentioned, in passing, the temporary improvement in the corrected suspension stability and sedimentation rate in some cases. I shall show how the blood picture as a whole is altered by blood transfusion, using the same examples and the same types as previously mentioned, i.e. (1) initial abnormal plasma proteins becoming normal after transfusion; (2) normal plasma proteins becoming abnormal after transfusion; and (3) normal remaining normal.

The normal figures we have taken for these factors are: Hæmoglobin 100% = 14 grammes %. Hæmatocrit 42-45%. Sedimentation rate (Wintrobe's method) 0-15 mm. in 1 hour (female); 0-10 mm. in 1 hour (male). Corrected suspension stability 85-95% in 1 hour (Spa Hospitals method).

On the graphs will be seen the hæmatocrit, hæmoglobin and the corrected and crude suspension stability rates. The crude sedimentation rate by Wintrobe's method paralleled almost exactly the suspension stability values. In all these cases blood transfusion resulted in a rise in the hæmatocrit and hæmoglobin values. The crude and corrected suspension stability improved temporarily with the lessening of anæmia and improvement of the plasma protein picture. At the same time the general condition of the patient improved markedly.

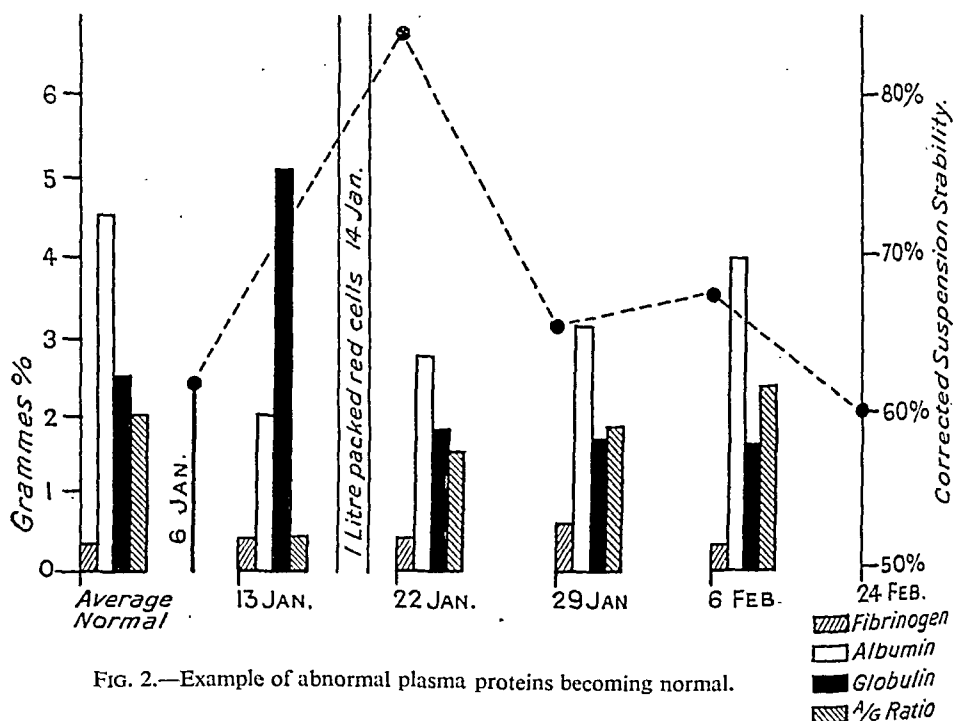


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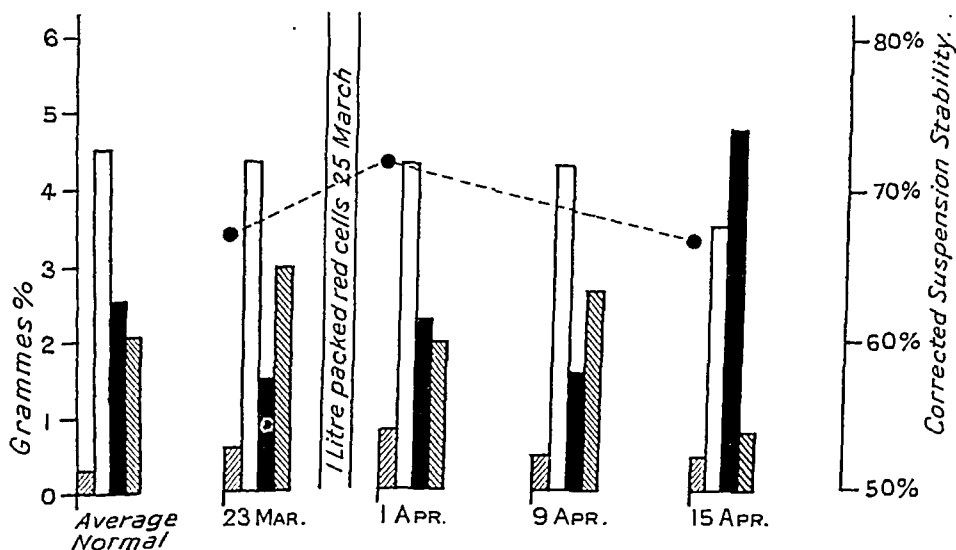


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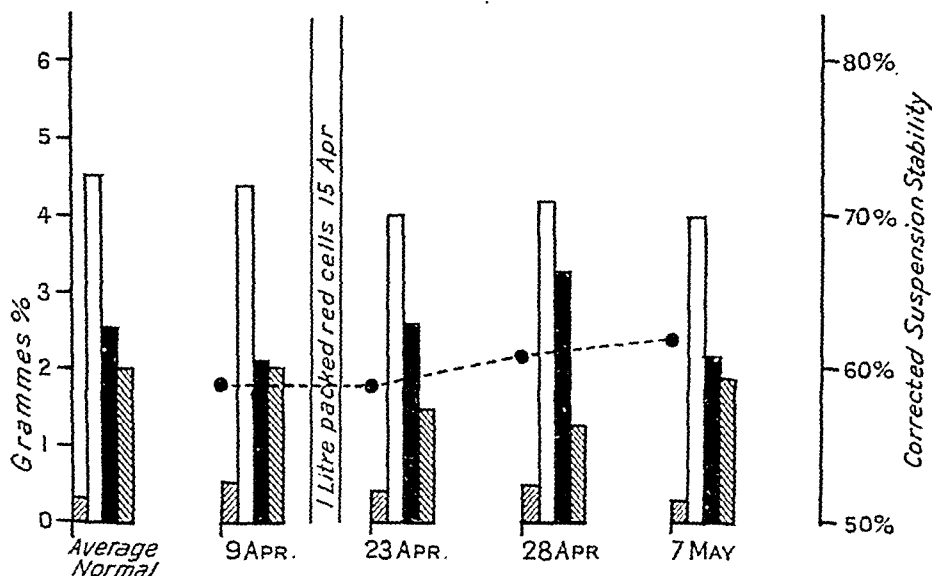


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Chart I is an example of initial abnormal proteins becoming normal after transfusion. It will be noticed that hæmatocrit, hæmoglobin and suspension stability, both crude and corrected, all improved temporarily and that four weeks after transfusion, the hæmoglobin and hæmatocrit were still higher than on admission, but the corrected suspension stability had returned to the original abnormal value. The maximal improvement, both clinical and biochemical, occurred seven to ten days after transfusion, after the plasma proteins had returned to within normal limits. The next chart is of the second type where initial normal plasma protein readings temporarily became abnormal after transfusion.

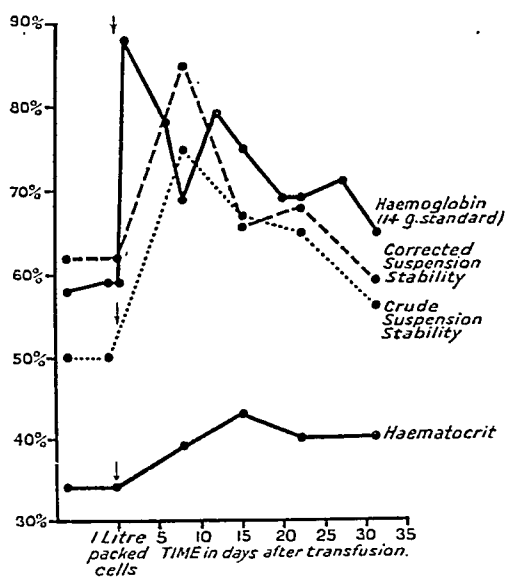


CHART I.—Abnormal plasma protein values becoming normal after transfusion.

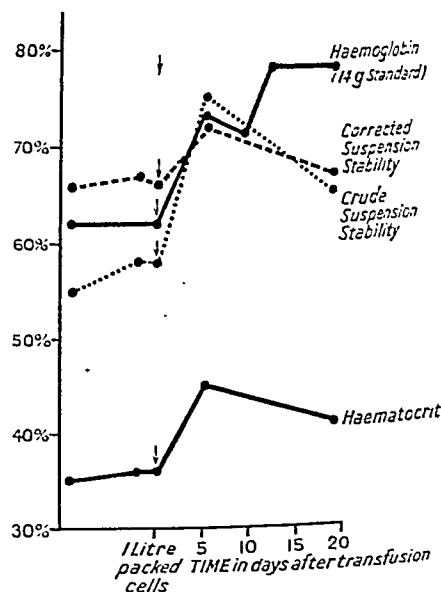


CHART II.—Normal plasma protein values becoming abnormal after transfusion.

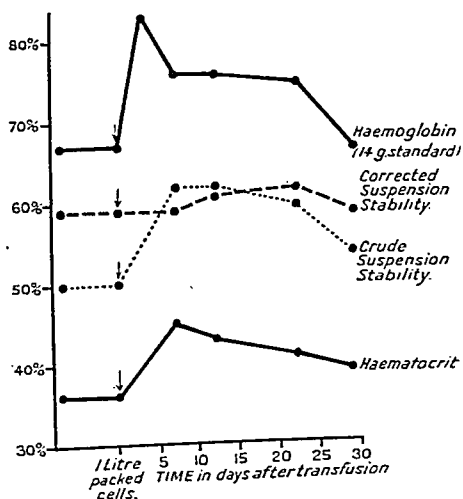


CHART III.—Normal plasma protein values before and after transfusion.

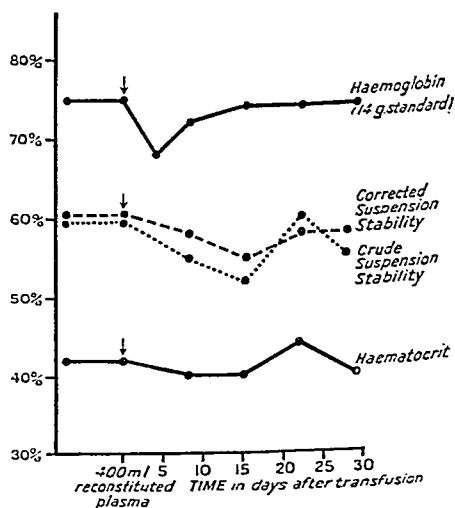


CHART IV.—Plasma transfusion.

In Chart II a rise in hæmatocrit, hæmoglobin and suspension stability occurred, but whilst the hæmoglobin was still maximal as a result of transfusion, the crude and corrected suspension stability values and hæmatocrit had dropped, coincident with the change to abnormal

albumin and globulin values. The fibrinogen readings, however, remained unchanged.

In Chart III an example will be seen of the third type where normal plasma protein values remain normal after transfusion. There is a rise in the hæmatocrit, hæmoglobin and crude suspension stability, but the corrected suspension stability remains substantially the same throughout the five weeks during which the case was under review.

Effects of transfusion.—*Subjectively:* The patients state that the pain was a little easier and they have less stiffness and more energy, feeling stronger in themselves and they find they are less easily fatigued and less depressed. *Objectively:* Trophic and other peripheral changes appear to be considerably improved. There is little or no obvious change in the appearance of the joints, either clinically or radiologically. The blood picture shows evidence of at least temporary improvement.

Chart IV is an example of one of the two cases which received 400 ml. of reconstituted plasma. It will be seen that there is little change after transfusion.

This is only the preliminary work, and we do not wish to draw any conclusions from the small number of results so far obtained. It is our intention to continue these studies with adequate normal controls for all the biochemical and hæmatological methods used and attempt to discover what constituent of blood is responsible for the improvements noted. The follow-up period of one month has been so limited because this hospital admits patients for an average duration of only six weeks, but these patients are being readmitted at regular intervals for further observation.

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Gout: a Case showing Unusually Rapid Progress.—G. D. KERSLEY, F.R.C.P.

Dr. G. D. Kersley showed a case of gout in a young man aged 23, who gave a history of two attacks in his left knee, five years previously. Four years ago the condition became chronic with acute exacerbations, the hands and feet also becoming affected. Shortly after this, tophi appeared first on the ears and then on the hands and feet. Two years ago, when first seen at the Royal National Hospital for Rheumatic Diseases, he showed deformity with ulnar deviation and swelling of his hands and swollen ankles and feet. He had lost a great deal of weight, was anæmic and had a plasma uric acid of 16 mg.% (blood urea 44 mg.%). In the past, gold therapy had made the condition worse and a muscle biopsy had shown no evidence of any rheumatoid factor. There was no family history of gout. He reacted well to colchicine and was controlled on a low-purine low-fat diet and extra fluids, after elimination of gross dental sepsis, the application of splints and sedative eliminative physical treatment. Since his first admission he has had several relapses, life being only bearable while he took colchicine, and when this was withdrawn on one occasion, he was admitted in a critically ill condition, with a temperature of 102° F., dehydrated, and with acute pain and swelling of both hands and both feet. Atophan appeared to have little effect in controlling the condition. The biochemical findings were—plasma uric acid 16 mg.%, blood urea 44 mg.%, sedimentation stability 58% (maximal), hæmoglobin 49%, W.B.C. 9,800, cholesterol 50 mg.%.

Dr. Kersley outlined the criteria which, in this case only when taken together, were diagnostic of gout—the acute onset, complete remissions in the early stages, the raised plasma uric acid, X-ray changes, reaction to colchicine and later the appearance of tophi—also the value of the negative muscle biopsy. Unusual factors in a case with a comparatively short history were the marked loss of weight, the anæmia and the absence of family history of the condition. He outlined in this connexion the work of Talbot on sex linkage of a hereditary factor in rise of blood uric acid (occurring in 25% of the non-gouty relatives of gouty patients, 80% of those with high blood uric acid levels being males).

No trigger factors—particular foods, sensitivity to sepsis, trauma or worry—had been discovered in this case. The value of colchicine in small dosage between attacks—a

Chart I is an example of initial abnormal proteins becoming normal after transfusion. It will be noticed that hæmatocrit, hæmoglobin and suspension stability, both crude and corrected, all improved temporarily and that four weeks after transfusion, the hæmoglobin and hæmatocrit were still higher than on admission, but the corrected suspension stability had returned to the original abnormal value. The maximal improvement, both clinical and biochemical, occurred seven to ten days after transfusion, after the plasma proteins had returned to within normal limits. The next chart is of the second type where initial normal plasma protein readings temporarily became abnormal after transfusion.

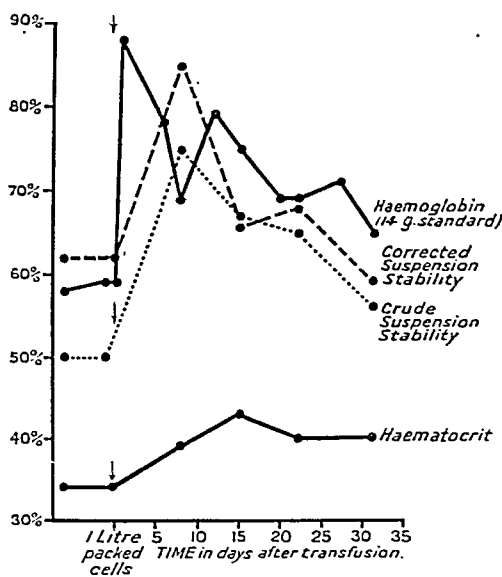


CHART I.—Abnormal plasma protein values becoming normal after transfusion.

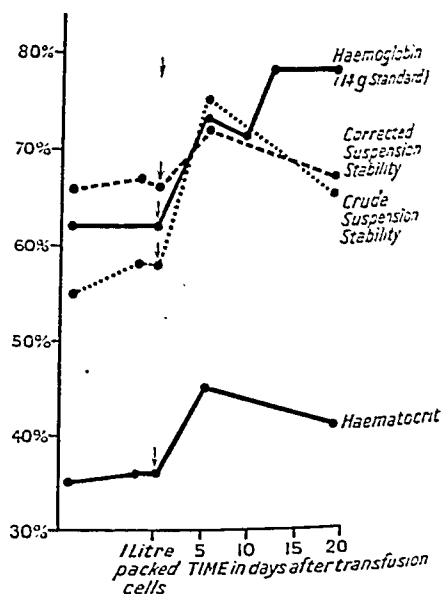


CHART II.—Normal plasma protein values becoming abnormal after transfusion.

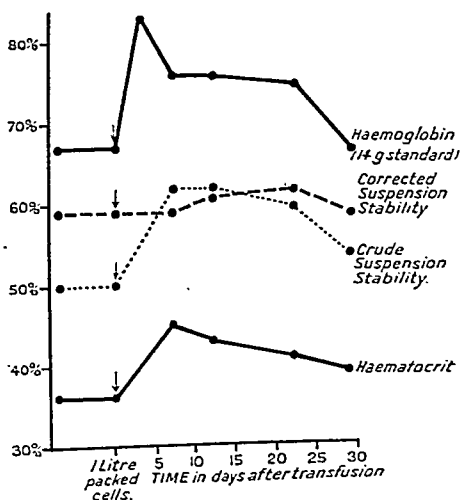


CHART III.—Normal plasma protein values before and after transfusion.

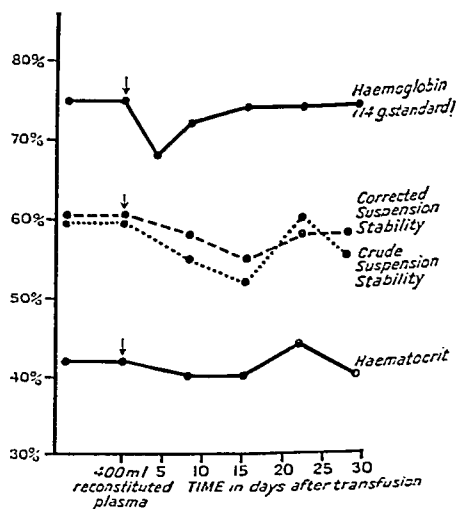


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therapeutic principle becoming more widely recognized lately—was well borne out in the progress of the case. The danger of colchicine idiosyncrasy must be recognized as a rare complication to the initial administration, but mild toxic symptoms of diarrhoea should act as a guide to a decision on the correct full dosage to be used in an acute attack for any individual patient.

Gold Dermatitis (Two Cases).—J. B. BENNETT, M.B., Ch.B.

Two cases of gold dermatitis treated by B.A.L. were recorded by Simpson (Simpson, N. R. W., 1948, *Brit. med. J.* (i), 545). The second of the two cases was shown at the Section Meeting.

The patient was admitted to the Royal National Hospital for Rheumatic Diseases, Bath, on November 12, 1946. He was a man of 43 years and showed typical signs of early rheumatoid arthritis of about twelve months' duration. The diagnosis was upheld by the hæmatological findings, i.e. B.S.R. by Spa Method 54%.

He was given intramuscular injections of myocrysin to a total of 0.66 gramme and was discharged in January 1947 with a request to his private doctor to complete the course to a total of 1.0 gramme. After receiving 0.86 gramme he developed an extensive and severe exfoliative dermatitis.

He was readmitted to hospital on 3.6.47. He had then complete acute dermatitis but his arthritic symptoms had entirely disappeared and his B.S.R. was 92%. He had regained his normal weight. Treatment of his skin by ordinary methods was of no avail. He was discharged on 14.7.47.

The patient was readmitted on 21.10.47 when it was found that the skin had become grossly indurated and was desquamating freely. The arthritic symptoms were in abeyance and the B.S.R. was 88%. Treatment by B.A.L. was then instituted on 24.10.47 and after about six days considerable improvement was observed. The skin became paler and the exfoliation, which had previously necessitated diurnal sweeping of his bed, almost entirely stopped. In all he was given 56 ml. starting with 2 c.c. four-hourly on the first day, twice daily for three days, daily for eleven days, alternate days for eight days.

He was discharged on 3.12.47. His skin had ceased to desquamate and had become soft although still discoloured with a violet hue.

He was readmitted on 16.3.48. There were no clinical signs of arthritis although the patient complained of some pain and stiffness in the left shoulder. His B.S.R. was 94%. Apart from some violet pigmentation of the skin of his abdomen and thighs there were no other residual effects of the dermatitis. The patient remarked that he had had an abscess of the buttock as a result of the B.A.L. injection but regarded it as of no consequence compared with the relief of his skin trouble.

The clinical result of the myocrysin injection was entirely satisfactory in that a complete cure was apparently effected. The patient will be kept under observation for some years.

Gold dermatitis is a devastating complication for both patient and doctor. The condition may drag on for months and months in spite of all efforts to control it. In this particular case B.A.L. undoubtedly produced an immediate and lasting improvement, with the prospect of return of the skin to complete normality.

Gold, which at present is considered to be the most effective drug in the treatment of rheumatoid arthritis, is quite rightly regarded as potentially dangerous. Of the three most important complications, i.e. blood dyscrasia, nephritis and exfoliative dermatitis, the last-mentioned would now appear to be controllable.

The patient here referred to is in no doubt that the price he paid in discomfort from his skin was well worth the relief of his arthritis.

Ankylosing Spondylitis.—H. LOVELL HOFFMAN, M.D.

Dr. Hoffman showed a case of ankylosing spondylitis and discussed the methods of treatment used for this disease at the Royal National Hospital for Rheumatic Diseases.

He explained that treatment consists of: (a) A plaster bed in which the patient rests for the greater part of the day. This is renewed after several weeks, when the spine has become straighter. (b) Deep X-ray treatment which almost invariably relieves pain and consequent muscle spasm. (c) Movements to the large joints such as hips, knees, and shoulders in the Hot Pool. (d) Breathing exercises also in the Hot Pool, the results being

controlled by periodic measurements of vital capacity and chest expansion. (e) When these measures have controlled pain and deformity, and the disease is becoming less active, a modified Goldthwaite brace is fitted, to be worn during that part of the day when the patient is not on his plaster bed.

Regarding the merits and demerits of preserving spinal mobility by forced active movements, his view was that except in those cases where involvement of the spine is minimal and there is a considerable degree of residual movement, ankylosis should be allowed to occur in the best possible position. In a patient with a stiff spine the burden of any forced movement is likely to fall on one particular intervertebral joint as a fulcrum. This can only, in his opinion, increase the activity of the disease.

In order that the recommendations made in hospital can be carried out, it is necessary to enquire into the patient's home conditions, and to enlist the aid of social and health organizations in the district.

Indications for Joint Manipulation

By JOHN BASTOW, M.D., F.R.C.S.

THE three chief indications for the manipulation of a joint are pain; limitation of movement; deformity; but before embarking on any such procedure, it is wise to make sure that there is a reasonable chance of success and none of disaster supervening.

The first essential before undertaking a manipulative operation is to make a correct diagnosis by (a) careful clinical history—stressing mode of onset and progress of case; (b) thorough clinical examination; (c) X-ray examination; (d) laboratory tests, especially blood sedimentation rate.

Neglect of these elementary precautions may lead to such tragedies as the following:

(1) A child with a "ricked neck" after fishing, due to turning his head suddenly when his cast became caught up in a tree behind him—an injudicious manipulation to free his "locked" neck was followed by a high temperature and an early death, due to pyæmia.

The case was one of "spontaneous hyperæmic dislocation of the cervical spine" following an attack of tonsillitis, and manipulation caused rapid dissemination of the infection and septicæmia.

(2) A boy with a "peroneal spasm" and a painful flat foot—manipulated to restore mobility—with the result that there was an acute flare-up of a latent tuberculous synovitis of the subastragaloid joint, followed by sinus formation and a long illness, the patient being fortunate to recover with an ankylosed foot.

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Such stories could be multiplied and serve to remind us that the art of the manipulator demands constant vigilance; that in no case can one afford to relax the essential precautions enumerated above, which can be summed up as "establish a diagnosis" in every case. Never manipulate "on spec".

Now supposing the diagnosis to have been established, what type of case does respond well to manipulation?

(1) The most successful cases are those following "minor trauma".

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Where the adhesion does not lie in the synovial membrane or capsular ligaments of a joint but in the attachment of a tendon or muscle, or between a tendon and its synovial

sheath, manipulation without anaesthesia is more effective, as the patient's involuntary resistance to the movement is essential to the success of the operation.

For example: (a) "*Tennis elbow*", affecting origin of extensor tendons of forearm. (b) Tendon adhesions in the long head of the biceps or in the extensor tendons of the wrist. (c) Adhesions between the small muscles of the back.

In such cases, the tissues are otherwise normal and a normal range of movement may be expected to be obtained.

(2) *Post-fibrositic stiffness*—either following an acute attack of fibrositis, which has subsided leaving some loss of function or persistent pain, or else as the sequel of long-continued chronic fibrositis. Usually the osteopath's spinal lesion is of this type—especially affecting the joints of the neck, the shoulders and the lumbar spine, and again a full range of movement may be obtained.

(3) In a similar category are the stiff neck following brachial neuritis and the stiff shoulder following adhesive pericapsulitis, but only when the acute stage has subsided.

Here it is usually wise to warn the patient that two or three serial manipulations may be required, and some temporary exacerbation of symptoms may follow each operation.

(4) *In osteo-arthritis* manipulation is of definite value, but great care must be taken to study the radiographs and attempt to regain only such a range of movement as the alteration in the contour of the articular surfaces and the contractures in the surrounding muscles and ligaments will allow.

Each manipulation must be followed by conscientious active exercises on the part of the patient, if any improvement gained by the movement is to be retained.

The deep Hot Pool bath with an attendant in the water to assist in the patient's movements is especially valuable in this condition.

Hips, shoulders, knees and spinal joints respond well on the whole.

(5) *In rheumatoid arthritis*, manipulation should never be employed in the acute stage with the idea of increasing movement of a joint. It may be used to correct flexion contracture if the joint is immediately immobilized by splintage in the corrected position, with the proviso that after twenty-four hours the splint is removed for a period daily to allow active movement and so prevent the development of ankylosis.

In the chronic stage, manipulation is often of value in increasing the range of movement of a stiff joint, but the radiograph must first be carefully studied to determine the amount of articular erosion that has taken place.

A full, normal range of movement can hardly ever be expected, and so manipulation must be guarded and no more force employed than the decalcified bones and fibrotic extra-articular tissues will stand.

Serial manipulations—only about 15% to 20% increase in movement being attempted at each stage—are very useful in this condition. Joints that respond well are shoulders, cervical joints, knees and feet. Elbows do not respond well and should rarely be manipulated in rheumatoid arthritis.

(6) *In gout*, manipulation must never be performed in the acute stage, and should only be used under an umbrella of colchicine in the quiescent stage, for fear of an acute flare-up.

Serial movements, especially active assisted movements in the Deep Pool, are usually the safest to employ.

Section of Otology

President—DONALD WATSON, F.R.C.S.

[May 7, 1948]

Lempert Fenestra Nov-Ovalis for the Restoration of Practical Unaided Hearing in Clinical Otosclerosis: Its Present Status¹

By JULIUS LEMPert, M.D., New York, U.S.A.

WHEN I first became interested in the surgical treatment of clinical otosclerosis I decided to direct my efforts towards developing and perfecting this surgery to a degree high enough to render its use by the otologist practical and its benefits to the deafened patient desirable and durable. It soon became obvious to me that to reach this objective I would have to:

(1) Create a technically safe and practical one-stage surgical procedure for the restoration of practical hearing in clinical otosclerosis.

(2) Find means for ascertaining preoperatively the likelihood of obtaining practical, serviceable and unaided hearing in a deafened ear following the use of such a technique.

(3) Find definitely prescribed ways and means of assuring the permanency of the practical hearing improvement once obtained following such surgical intervention.

In *Archives of Otolaryngology* (1938, 28, 42-97) I described the first practical one-stage fenestration technique for the improvement of hearing in clinical otosclerosis. During the last ten years I have developed many technical improvements in the surgery for clinical otosclerosis. These were based upon a continuous study and analysis of the various results obtained following 3,700 fenestration operations which I have performed, the observations I have made during the performance of 450 revisions and the histologic findings of scientifically controlled animal research.

The restoration of practical hearing following fenestration surgery was observed to be influenced by factors of preoperative, operative and postoperative origin.

PREOPERATIVE FACTORS INFLUENCING THE RESTORATION OF PRACTICAL HEARING

The preoperative diagnosis of clinical otosclerosis is not difficult. In performing the fenestra nov-ovalis operation stapedial foot-plate ankylosis has been observed in almost 100% of cases diagnosed as clinical otosclerosis.

In the only two cases that later came to autopsy of irrelevant causes the otosclerotic lesion was histologically present.

The fenestration operation serves those deafened as a result of otosclerosis best, when their preoperative cochlear nerve function reservoir has remained adequate enough to permit the restoration of practical serviceable unaided hearing.

If the restoration of practical hearing in clinical otosclerosis is to be the objective of the fenestration operation it is essential that the preoperative bone conduction hearing for the 512, 1,024 and 2,048 pure tone frequencies should not be lower than the 30 decibel level and that the decibel level of the bone conduction hearing should be at least 25 to 30 decibels higher than the decibel level of the air-conduction hearing.

Experience has shown that an improvement in hearing for air-conducted sound following fenestration must reach at least the 30 decibel level in the 512, 1,024 and 2,048 frequencies to be considered as serviceable enough for social and economic purposes and obviating the necessity of wearing a hearing aid.

Hearing can be restored to the practical level or higher, even as high as the normal level by the fenestration operation, providing the reservoir of unused cochlear nerve

¹The Paper was followed by the projection of a colour film illustrating every detail of the operation.

function still present at the time of operation is sufficient to permit such restoration of hearing. In the presence of an adequate cochlear nerve function reservoir the degree of the preoperative hearing loss for airborne sound, no matter how great, will nevertheless not interfere with the restoration of practical hearing.

The correct determination preoperatively of the cochlear nerve function reservoir remaining untapped by the functionally impaired air-conduction mechanism is not difficult if the otologist possesses a good old-fashioned clinical sense plus an appreciation of the psychology of the deafened. By supplementing the audiometric testing with intelligent use of the old-fashioned 512, 1,024 and 2,048 frequency steel tuning forks for testing bone conduction hearing for pure tones, plus the use of the outmoded speaking tube for testing the intelligibility for the spoken voice, the otologist can obtain much more valuable information as to the possibility of restoring practical hearing with the fenestration operation in a given ear than by accepting the reports of conclusions reached by physicists and acoustic engineers with the use of extremely complicated apparatus in their psycho-acoustic laboratories.

No otologist should perform a fenestration operation without first personally testing the patient to determine his chances for the restoration of practical hearing. He must never operate solely on the findings of another otologist.

Though the need for newly developed accurate tests for differentiating between middle and inner ear deafness is greater to-day than ever before, only the development of simple non-complicated tests practical enough for the average otologist to employ in his office will be acceptable in the long run.

If, following a well-performed fenestration operation, an impressive hearing improvement cannot be audiometrically demonstrated despite the presence of a strongly positive response to the fistula test it may be concluded that the cochlear nerve function reservoir was incorrectly evaluated preoperatively. It would be highly speculative to deduct from such a result, which is not uncommon, that in addition to the preoperatively diagnosed stapedia foot-plate ankylosis there also must exist in such a case an obstructive otosclerotic lesion in the region of the round window membrane. Histologically otosclerotic lesions in the round window niche, sufficient to interfere with the mobilization of the round window membrane by airborne sound, have been only rarely observed. Furthermore, the preoperative bone conduction hearing in such cases would not as a rule be found to be good enough to consider such an ear as suitable for the fenestration operation.

POINTS OF OPERATIVE TECHNIQUE WHICH INFLUENCE THE RESTORATION OF PRACTICAL HEARING

The creation of a new vestibular fenestra to replace the functionally impeded oval window results in improved mobilization of endolymph by airborne sound which in turn can result in the restoration of practical hearing if the existing cochlear nerve function is adequate.

A tympanic air-space hermetically sealed with the tympanic membrane is essential following fenestration so that the endolymph could be mobilized by airborne sound.

The fact that practical hearing cannot be restored by fenestration in the presence of a perforated tympanic membrane is suggestive that a hermetically sealed tympanic air space acts as a phase changer for the mobilization of the endolymph by airborne sound following the fenestration operation.

The newly created vestibular fenestra must be sealed with a viable tympano-meatal flap to protect the membranous labyrinth from degenerating with total loss of hearing resulting. Since mass influences the transmission of airborne sound to the perilymph space, the thinnest employable portion of the tympano-meatal flap should be facing the newly created vestibular fenestra.

The tympano-meatal membrane, though it is a continuous membrane, cannot

conduct a sound wave from the tympanic membrane to the cutaneous portion which covers the new fenestra. The maintenance of continuity between the dermal layer of the tympanic membrane and that of the cutaneous portion of the tympano-meatal flap is essential for reasons apart from sound transmission. To assure the survival of the cutaneous portion of the tympano-meatal flap it is essential that it be nourished by the blood supply of the tympanic membrane.

The intermediate portion of the tympano-meatal flap becomes firmly adherent to bone between the tympanic air-space and the newly created vestibular window and therefore does not permit airborne sound striking the tympanic membrane to be transmitted effectively to the cutaneous portion sealing and covering the new fenestra. Further proof that mobilization of the tympano-meatal membrane as a whole and transmission of sound waves from its tympanic membrane to the fenestra segment does not take place following fenestration is the fact that practical hearing can be obtained when the cutaneous portion of the flap is accidentally severed from the tympanic portion, providing the cutaneous portion is replaced and adheres so that both the tympanic air-space and the newly created window remain hermetically though independently sealed.

Sound most likely enters simultaneously and independently both the round cochlear window and the newly created vestibular window and mobilizes the endolymph out of phase. It enters the round window through the tympanic portion of the tympano-meatal membrane and the new oval window through that part of the cutaneous portion of the tympano-meatal membrane which covers and seals it.

Since part of the tympano-meatal membrane remains adherent to bone and is therefore not mobilizable as a whole by airborne sound, the maintenance of the incus in its original position after removing the head and neck of the malleus can serve no useful acoustic purpose because it cannot act to enhance the mobilization of endolymph by airborne sound. The fenestra nov-ovalis operation has conclusively proven that just as good, or better, improvements in hearing are obtainable since incus is being removed.

By the same token neither is the retention of the mucous membrane covering the tympanic portion of the facial canal necessary since it cannot result in better post-operative hearing.

The absence of an audiometric hearing improvement for airborne sound coupled with a negative response to the fistula test following the fenestration operation is usually the result of accidental surgical injury to the membranous external semi-circular canal.

POSTOPERATIVE FACTORS INFLUENCING RESTORATION OF PRACTICAL HEARING

A further loss in the hearing level following the fenestration operation in the presence of a negative fistula test may as a rule be attributed to severe postoperative labyrinthitis. Extensive injury of the perilymphatic trabecular blood-vessels, the creation of the fenestra in the presence of bleeding from the mastoid wound, the sealing of the fenestra with the tympano-meatal flap in the presence of bleeding, excessive postoperative inflammation or infection of the tympano-meatal flap, any of these could at one time or another be the responsible factor for such an untoward result.

However, postoperative labyrinthitis is to-day no longer a problem of this surgery. The meticulously careful performance of the fenestration operation with instantaneous surgical control of each and every bleeding point, when supplemented by daily administration of 300,000 units of penicillin for a period of ten postoperative days, has reduced the frequency of postoperative labyrinthitis with resulting further loss of hearing to less than 1%. Penicillin, by reducing postoperative inflammation of the tympano-meatal flap to a minimum, in addition to its antibiotic action, has made this possible where all other means including the sulpha drugs have failed.

POSTOPERATIVE FACTORS INFLUENCING THE PERMANENCY OF RESTORED PRACTICAL HEARING

A drop of the air-conduction hearing level in the three speech frequencies from the best postoperative level to a level below that necessary for practical hearing is as a rule representative of osteogenesis taking place within the fenestra rim. Though the hearing recession may not yet have reached the preoperative level it will ultimately decline to that level when bony closure of the fenestra is sufficiently advanced.

When the improved postoperative hearing level does not show a tendency to drop, a negative response to the fistula test is not a sign of bony closure. However, when the hearing level shows a tendency to drop below the practical level, a positive fistula test is no proof that window is not undergoing bony closure, since a positive fistula test is obtainable even when the newly created fenestra is reduced to the size of a pin-point.

An otologist doing fenestration surgery cannot possibly acquire an appreciation of the complexity of the problems involved in this surgery, nor hope to improve himself or the surgery itself unless he insists upon revising and carefully studying his failures.

Repeated revisions of an osteogenetically closed fenestra do not as a rule result in a permanently open window, and endanger the well-being of the endolymphatic labyrinth.

Though the frequency of osteogenetic closure of the newly created fenestra has been greatly reduced since the general adoption and employment of the fenestra nov-ovalis operation its occurrence is, however, not yet as infrequent as some otologists believe it to be.

If this surgery is done with an open mind and with a critical evaluation of results the occurrence of window closures will inevitably be recognized. However, if one's mind is shut to this surgery and one is easily satisfied with the results obtained, then nothing but open windows will be seen.

Careful study of the newly created fenestra region in the post-fenestrated human subjects during revisions and the histologic observations made in the experimentally controlled post-fenestrated rhesus monkeys have shown that when osteogenesis takes place following fenestration it does so either in the region of the fenestra rim or in the perilymph space and also in both the fenestra rim and the perilymph space.

Further investigation of this problem has revealed that osteogenetic closure of the new fenestra is influenced mainly by:

(1) *The site chosen for the creation of the fenestra.*—As a result of careful analysis of the observations made during revisions of osteogenetically closed fenestras in post-fenestrated human ears I developed the fenestra nov-ovalis technique which I described in November 1941 (*Archives of Otolaryngology*, 34, 880-912).

By changing the fenestra site and moving it forward over the ampulla of the external semicircular canal and immediately anterior to it—which region forms the surgical dome of the vestibule—one of the great factors responsible for osteogenetic closure of the newly created fenestra is removed.

A fenestra created in this region communicates directly with the perilymphatic cisterna of the vestibule which is 3 mm. wide and 5 mm. deep. The formation of a fibrous connective tissue matrix which could aid and abet osteogenetic closure of the fenestra is less likely to take place in this region than in a fenestra created posterior to the ampulla of the external semicircular canal into a perilymphatic space the circumference of which is only about 0.8 mm.

The universal adoption and employment of the fenestra nov-ovalis technique has for the first time in the history of this surgery sharply reduced the frequency of osteogenetic closure of the newly created fenestra.

(2) *The inherent natural tendency for osteogenetic repair of the freshly injured histologic bony layers of the fenestra rim.*—In a discussion of osteogenesis following the fenestration operation in the human (*Archives of Otolaryngology*, 1940, 31, 711-779) I stated as follows:

From my observations during revisions of the fenestra, I was forced to conclude that new bone regeneration within the fenestra begins not in the periosteal but in the endosteal layer of the bony capsule and either may stop there, without involving the periosteal layer, or may eventually involve the periosteal layer of the bony walls of the fenestra.

Fig. 1 shows the three histologic layers of the labyrinthine bony capsule.

In the November 1947 issue of the *Archives of Otolaryngology*, 46, 590, Lindsay, in an analysis of his histologic observations of the results following fenestration of the labyrinth in the rhesus monkey, corroborated the observations which I have made in the human and stated as follows:

Failure to maintain an open fistula was in most cases due to the osteogenetic process which took origin from the endosteal surface at the margins.

Fig. 2 shows closure of the fenestra caused by osteogenetic repair of the endosteal bony layer only.

Neither the removal of the periosteal layer down to the enchondral layer of the bony fenestra rim, nor the removal of both the periosteal and enchondral layers of the fenestra rim down to the endosteal layer, prevents bone regeneration of the endosteal layer. Whether bony closure of the fenestra is the result of endosteal osteogenesis alone or osteogenesis involving all the three histologic layers is quite immaterial as to its effect upon the end-result. None of the three histologic layers is immune to osteogenesis. This has been amply demonstrated histologically in the rhesus monkey.

Scientifically controlled experimentation in the rhesus monkey has demonstrated that burnishing the fenestra rim with pure lead inactivates the histology within the freshly injured bony fenestra rim and prevents osteogenetic closure of the fenestra (*Arch. Otolaryng.* (1947) 46, 512-527).

The use of lead burnishing in 800 consecutive patients since December 1947 seems to be corroborative of our experimental findings in the rhesus monkey.

In only 5 of the 170 cases which are now more than one year postoperative is there any apparent clinical evidence of bone regeneration. However, one more year will have to pass before final evaluation of the lead-burnishing technique can be made.

Prior to the use of lead burnishing signs and symptoms of bone regeneration at the end of one year would be discernible in about 25% to 30% of the cases.

(3) *Bone dust and bone splinters left behind in the region of the fenestra gap and within the perilymphatic space.*—In the surgical treatment for clinical otosclerosis, bone sand and bone splinters have always been by-products of fenestrating the bony labyrinthine capsule with the electrically driven burr. When the final endosteal bony layer is fractured inward and pulverized, bone dust and bone splinters are pushed in the direction of the perilymph space with most of them coming to rest upon the shredded endosteal membrane and the endolymphatic labyrinth. It has been a well-recognized fact that when these bone particles are not meticulously removed from the fenestra region they may stimulate and enhance the naturally existing tendency for osteogenesis in the freshly cut bony walls of the fenestra rim.

It is for this reason that various means of meticulously removing the fractured and pulverized endosteal layer of the bony capsule, which is seen resting upon the shredded endosteal membrane and the endolymphatic labyrinth, are being practised by otologists doing fenestration surgery.

However, every careful otologist practising fenestration surgery could not help

but observe that in fracturing and pulverizing the endosteal bony layer of the fenestra region, bone dust and bone splinters unavoidably fell into the perilymph space and frequently disappeared beyond sight and reach.

Lindsay, after having made similar observations following experimental fenestration surgery in the rhesus monkey, stated in the November 1947 issue of the *Arch. Otolaryng.*, 46, 590, as follows:

The histologic examination has demonstrated that although at operation the technique appeared to be carried out faultlessly the complete removal of bone dust and fragments was rarely accomplished.

Attempts at removal of bone splinters from the perilymph space often result in severance of some of the perilymphatic trabeculae with hæmorrhage from the trabecular blood-vessels into the perilymph space.

Figs. 3, 4, 5 and 6 show normally present perilymphatic trabeculae and trabecular blood-vessels in the vestibular labyrinth.

The endolymphatic labyrinth can easily be injured by a bone splinter left within the perilymph space or torn by attempts to remove such a splinter from the perilymph space.

Fig. 7 shows injury to endolymphatic labyrinth sustained as a result of bone splinters lost in the perilymphatic space of experimentally fenestrated rhesus monkey.

As a result of my careful observations in the performance of 450 revisions of fenestrated human ears, and the observations made in my histologic studies of the temporal bones in our experimentally fenestrated rhesus monkeys (*Arch. Otolaryng.* (1947) 46, 512-527), I am convinced that bone dust and bone splinters entering the perilymph space are a much more serious threat to the hope of obtaining and continuously maintaining practical serviceable hearing as a result of fenestration surgery than bone dust and bone splinters resting in the region of the fenestra rim. This is so because bony fragments lost in the perilymph space are often not removable, while bone particles in the region of the fenestra rim can, as a rule, be completely removed.

In my postoperative clinical study of the 3,700 fenestration operations which I performed, I was able to observe two distinct clinical pictures both of which could be indicative and suggestive of an osteogenetic process having taken place post-operatively.

Clinical Picture Number One

A patient who had practical hearing restored and after having maintained this improvement at that high level for six months to a year suddenly begins to lose his hearing again and slowly his hearing acuity returns to the preoperative level and remains more or less at this level for some time.

In the vast majority of patients presenting this postoperative clinical picture, inspection of the fenestra region during revisions revealed that bone regeneration was limited to the fenestra rim of the bony labyrinthine capsule. When the newly formed endosteal bony growth was removed from the fenestra rim the hearing, as a rule, immediately improved and when osteogenesis did not recur, this improvement continued indefinitely. If osteogenetic closure of the fenestra took place once again the hearing again receded to the preoperative level.

In some fewer cases belonging to this clinical group I found no bone regeneration in fenestra rim but observed some narrowing of perilymphatic lumen as a result of endosteal osteogenesis. In these cases the hearing showed no improvement following revision and not infrequently the hearing continued to recede still further following the revision.

Clinical Picture Number Two

A patient who had practical hearing restored following the fenestration operation at the end of six months or so begins to lose his hearing improvement and more or less rapidly reaches the preoperative hearing level, but instead of remaining at that level for some time, his hearing continues to deteriorate to a level lower than it was preoperatively.

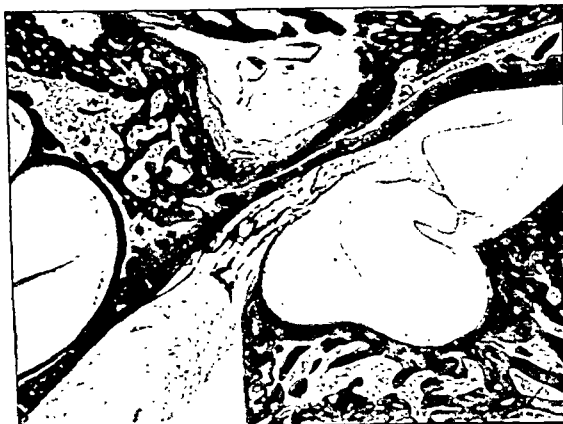


FIG. 1.



FIG. 3.



FIG. 2.

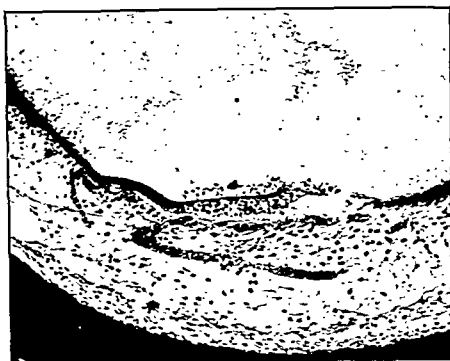


FIG. 4.

FIG. 1.—M. G. 10811. Right. Eight-month fetus. Three layers of bone form the otic capsule. A relatively thin layer of lamellar bone, the endosteal bone, immediately surrounds the membranous labyrinth. Next to this lies the more extensive enchondral layer, consisting of globuli interossei and marrow spaces. Most peripherally lies the periosteal layer of lamellar bone.

FIG. 2.—Osteogenetic closure of fenestra in rhesus monkey by endosteal bone only. The periosteal and enchondral layers are not participating in the process of osteogenesis.

FIG. 3.—Human 41—10811. Left. Eight-month fetus. Perilymphatic trabeculae and blood-vessels within vestibular labyrinth of eight-month-old fetus.

FIG. 4.—Human 35. Left. 254. Perilymphatic trabeculae and blood-vessels within external semi-circular canal of human labyrinth.

The findings grossly observed with the aid of magnification upon revision of the fenestra in such cases were usually of a more serious nature. Here the osteogenetic process was observed to have involved extensively both the fenestra rim and the perilymph space. The hearing in these cases did not improve following revision and continued its downward trend.

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basis, since injury to the endosteum-lined perilymphatic space is normally not part of my surgical technique. I therefore reasoned hypothetically that perhaps the perilymphatic endosteal osteogenetic processes which I observed in the human have been initiated by bone fragments having found their way unnoticed into the perilymph space.

Histologic studies of our experimental post-fenestrated rhesus monkeys have confirmed my suspicions that irremovable bone fragments, entering unavoidably and unnoticed and remaining in the perilymph space, do create endosteal osteogenesis in the perilymph space, a non-remediable condition which when occurring following the fenestration operation in the human is most damaging to the expected end-results.

Figs. 9, 10 and 11 show perilymphatic endosteal osteogenesis initiated by bone



FIG. 9.



FIG. 10.



FIG. 11.

FIG. 9.—Monkey 42. Left. Exp. III. 6 months 1 week P.O. Fenestra of fenestrated rhesus monkey has remained patent showing absence of osteogenesis at fenestra rim. However, perilymphatic endosteal osteogenesis stimulated by unavoidably lost bone particles within the perilymph space can be seen.

FIG. 10.—Monkey 46. Right. Exp. III. 3 months 2 weeks P.O. Almost complete obliteration of perilymphatic space of external semicircular canal in fenestrated rhesus monkey by endosteal osteogenesis which was apparently initiated by bone particles unavoidably lost in perilymph space during the process of fenestration. Osteogenesis has also taken place at fenestra rim.

FIG. 11.—Monkey 23. Left. Exp. II. Sec. 500. Complete obliteration of perilymphatic space of external semicircular canal in fenestrated monkey by endosteal osteogenesis which was apparently initiated by bone particles unavoidably lost in perilymph space during the process of fenestration.

fragments lost unavoidably within the perilymph space of the post-fenestrated rhesus monkey.

In view of the clinical and operating-table observations, made in the human following fenestration of the labyrinth for clinical otosclerosis and the histologic observations made in the post-fenestrated labyrinths of rhesus monkeys, it became obvious that just as long as the creation of the fenestra nov-ovalis will involve the

In analysing these findings in the two groups of post-fenestrated patients it became obvious that, since I have always meticulously removed all bone fragments visualized in the region of the fenestra gap, the osteogenetic process observed in the bony fenestra rim evidently was started by the inherently existing tendency for repair within the freshly injured bony histologic layers of the fenestra rim.



FIG. 5.—Human 10942. Right. Three-day infant. Perilymphatic trabeculae and blood-vessels within vestibule of human labyrinth.



FIG. 6.—Monkey L. I. 21. Right. Perilymphatic trabecular blood-vessels within crus commune of fenestrated rhesus monkey.



FIG. 7.—Monkey 24. Right. Exp. II. Injured endolymphatic labyrinth as a result of unavoidably lost bone splinters within the perilymph space of the external semicircular canal of a fenestrated rhesus monkey. Newly created fenestra is completely closed by osteogenesis.



FIG. 8.—Monkey 28. Right. Exp. II. Normally appearing perilymphatic space of fenestrated external semicircular canal in rhesus monkey. The endolymphatic labyrinth is seen in its normal position and uninjured. The perilymphatic trabeculae and blood-vessels remained uninjured and intact. Neither bone-dust nor bone-chips have entered the perilymph space. Bone regeneration has taken place only in the region of the fenestra rim.

Fig. 8 shows osteogenetic process limited to freshly injured bony walls of fenestra rim in post-fenestrated rhesus monkey. The perilymphatic space appears normal with the endolymphatic labyrinth and trabeculae undisturbed.

However, the endosteal osteogenetic processes observed within the perilymphatic space during revisions of post-fenestrated human ears could not be explained on this

the antero-lateral margin of the base of the endosteal bony cupola is engaged, gently lifted and everted in a direction postero-lateral to the fenestra and removed intact. The endolymphatic labyrinth, without having been disturbed from its normal position, is thus exposed to view (figs. 14A, B).

Step IV.—Lead-burnishing of bony fenestra rim. To prevent osteogenesis from



FIG. 13A.

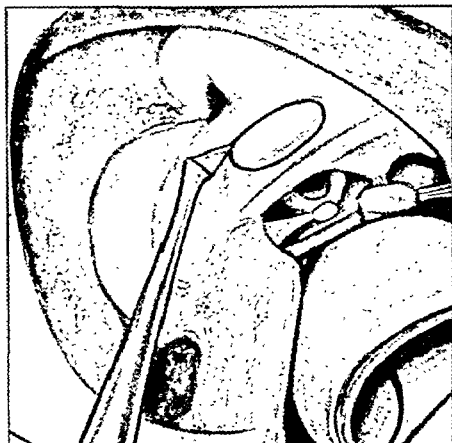


FIG. 13B.

FIG. 13A and B.—Step II: Base of bony endosteal cupola is circumferentially incised.

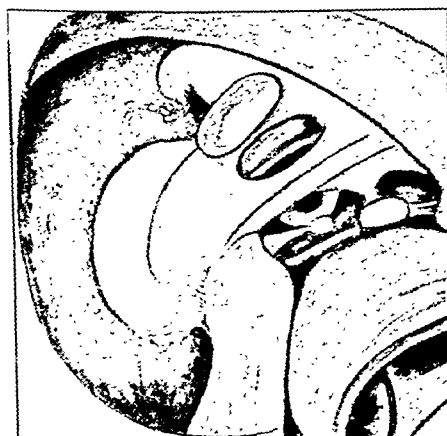


FIG. 14A.

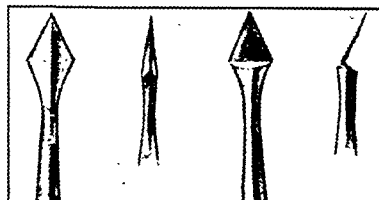


FIG. 13C.

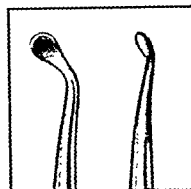


FIG. 14B.

FIG. 14A.—Step III: Eversion and removal of intact bony cupola to uncap perilymph space and expose to view endolymphatic labyrinth.

originating within the bone-dust-free freshly cut bony fenestra rim.—Pure lead is applied to the fenestra rim using a specially devised pencil holder. The leaded surface is then highly polished with an electrically driven smooth steel or gold burnishing burr.

ADVANTAGES

(1) By employing this new technique for creating the fenestra nov-ovalis, the endosteal bony layer of the labyrinthine capsule is neither fractured inward nor pulverized. Since no bone particles are formed, none can be lost in the perilymphatic space. Therefore, neither the endolymphatic labyrinth nor the trabecular blood-vessels are ever in danger of being injured by bone splinters.

fracturing inward and pulverization of the endosteal bony layer of the labyrinthine capsule, some of the bone splinters and bone dust thus formed will frequently fall into the perilymph space and unavoidably disappear beyond retrieve within it.

In order to avoid the dire consequences and untoward end-results observed, which were caused apparently by non-retrievable unavoidably lost bone fragments within the labyrinthine perilymph space, I have gradually developed a new technique which I now exclusively employ for fenestrating the surgical dome of the vestibule without creating bone splinters and bone dust.

BONE-DUST-FREE FENESTRA NOV-OVALIS TECHNIQUE

*Step I.—Creation of an endosteal bone cupola on surgical dome of vestibule (fig. 12).—*Employing an electrically driven 1 mm. dental polishing burr the bony capsule of the surgical dome of the vestibule is gradually worn down to the endosteal bony

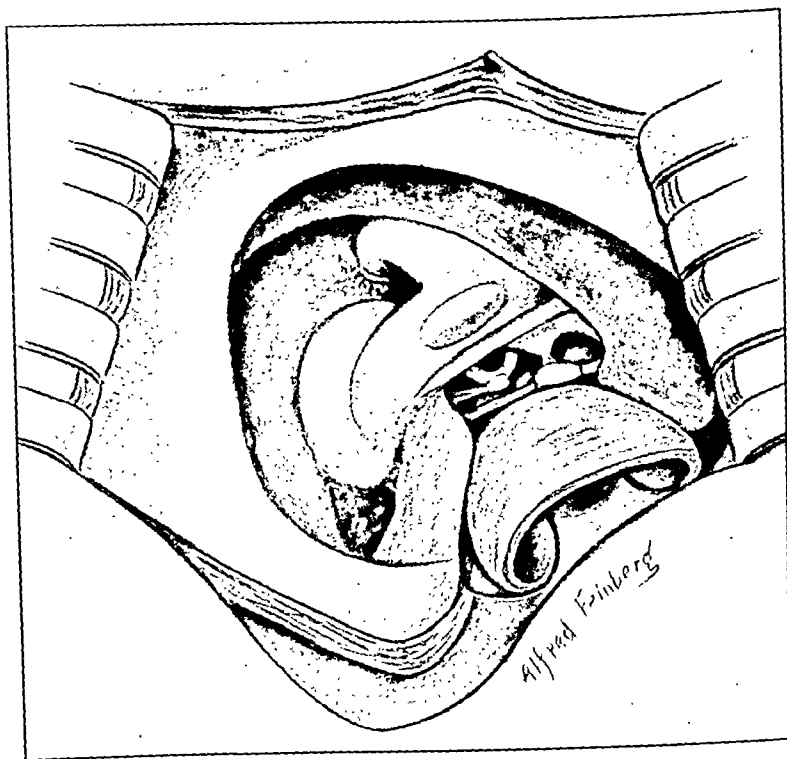


FIG. 12.—Step I: Creation of an endosteal bone cupola on surgical dome of vestibule.

layer, until it is thinned to a bluish-grey transparency. The bony capsule is then slowly and gradually worn down both antero-lateral and postero-lateral to the bluish-grey transparent area until a bluish-grey cupola of endosteal bone is created upon the surgical dome of the vestibule. The bone dust formed is constantly removed with saline and suction.

Step II.—Base of bony endosteal cupola is circumferentially incised.—In an absolutely blood-free surgical field, free from bone debris, the base of the cupola is incised as follows: The antero-lateral aspect of the base of the cupola is incised with a small sharp perforating knife in the direction of the perilymph space. A linear incision is then carried from the perilymph space outward through the endosteum and endosteal bone along the entire circumference of the base of the cupola (figs. 13A, B, C).

Step III.—Eversion and removal of intact bony cupola to uncap perilymph space and expose to view endolymphatic labyrinth.—With a flat spatula-tipped excavator

percentage of cases to render the surgical treatment of clinical otosclerosis acceptable to both the otologist and his patients.

There exists evidence now which suggests that the percentage of permanent practical hearing improvements is still further increased when the fenestra edges are treated with pure lead.

Also it is logical to assume that the bone-dust-free atraumatic creation of the fenestra will prove to be another great advance towards the final successful solution of the surgical treatment of clinical otosclerosis.

Mr. Terence Cawthorne, after congratulating Dr. Lempert on the brilliant presentation of his subject, went on to say that in the fenestration operation Dr. Lempert had done more than any other single person to help the hard-of-hearing and unlock the door of deafness; but he had done more than this, for not only had he found the key that unlocked the door, but he had given that key to others and taught them how to use it, with the result that there were many men all over the world to-day who had been trained by Dr. Lempert in the technique which he had shown to them this morning.

When he was in America the speaker had had the good fortune to see Dr. Lempert at work. During the all-too-brief week that he spent at Dr. Lempert's Institute he had learnt a great deal, and he wished Dr. Lempert to know how very much he appreciated all that had been shown to him and all that he had learnt, not only from watching operations, but from observing the care with which Dr. Lempert selected the patients and the infinite personal pains that he took over each case.

The demonstration of specimens in the West Hall of the Royal Society of Medicine illustrating temporal bone surgery enabled the details of the technique to be appreciated by anyone who had the time to study the specimens. He thought that they represented a magnificent achievement, not only on Dr. Lempert's part, but also on the part of Mr. Olofson, the technician, who had come over to England with Dr. Lempert and who played an important part in arranging and mounting the specimens.

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The Section was very glad indeed that Dr. Lempert was accompanied by Dr. Kos. Dr. Kos had been doing some very important otological work for the American Air Force during the war, and he came from the University of Iowa, which had always been famed for the part it had played in otology, as it was there that the pure tone audiometer was first developed.

The speaker asked if Dr. Lempert could tell them what was the chance of long-term improvement in hearing that a surgeon well trained in the fenestration technique could conscientiously offer to his patient; and, secondly, what steps Dr. Lempert would advise to combat the infection that so often persisted in the cavity after a fenestration operation.

Finally, Mr. Cawthorne paid a personal tribute to Dr. Lempert whom he was very proud to call his friend and also his colleague, for they both had the honour of being Fellows of the American Laryngological, Rhinological and Otological Society and also the great honour of being Honorary Members of the American Otological Society.

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Mr. I. Simson Hall, in seconding the vote of thanks, also expressed the great pleasure that it was to have listened to what Dr. Lempert had told them that day. An enormous amount of scientific research and clinical observation had gone to the elaboration of this method. All over the United States there were thousands of people to-day who had the happiness of hearing when previously they could not hear, and this was due, directly or indirectly, to Dr. Lempert's work. He thought that was the thing that must give him the greatest satisfaction.

One of the most important contributions which Dr. Lempert had made to this operation was his demonstration that it was capable of being done safely in one stage.

There was a class of case in which it was very difficult to decide whether or not to advise operation. It was a type of patient who had a reasonably good bone conduction for the speech range but by reason of trauma or of other damage to the cochlea had a sharp drop in hearing at the upper level of speech. In such a border-line case, how did Dr. Lempert assess such a patient?

The President, in associating himself with what Mr. Cawthorne and Mr. Simson Hall had said,

(2) Since there are no bone particles to be lost in the perilymph space, endosteal osteogenetic processes formerly stimulated in the perilymph space by such bone particles are no longer possible.

(3) By employing this technique the endolymphatic labyrinth always maintains its normal position within the perilymph space.

(4) Fenestration surgery can thus be performed without traumatizing the endolymphatic labyrinth, the trabeculae and endosteal perilymphatic membrane.

By employing the bone-dust-free technique for creating the fenestra nov-ovalis the heretofore existing problem of how to best accomplish the removal of bone dust has been disposed.

EVALUATION OF RESULTS FOLLOWING FENESTRA NOV-OVALIS OPERATION

A uniformly agreed upon method of evaluating and reporting results is desirable. Careful postoperative testing with pure tone audiometry and its comparison with the preoperative audiometric reading are to date the most scientific means of evaluating the hearing result obtained.

A patient's postoperative claim of improved hearing acuity following the fenestration operation is acceptable only when his claim can be audiometrically substantiated, just as his preoperative claim of deafness was substantiated audiometrically.

Though it is true that preoperative pure tone air-conduction hearing for the 512, 1,024 and 2,048 frequencies at the 30 decibel level in a deafened ear does not necessarily always represent practical serviceable hearing for the spoken voice, it is only a half-truth, since it is also a fact that in such an ear the cochlear nerve function as represented by the bone conduction hearing is already at a level lower than the air-conduction hearing. However, a postoperative rise in the pure tone air-conduction hearing to the 30 decibel level, from a preoperative lower decibel level, following the fenestration operation is always accompanied by improved intelligibility for the spoken voice and is therefore representative of practical hearing. Such a pure tone decibel improvement and improved intelligibility could not have taken place if the bone conduction hearing representing the cochlear nerve function reservoir was not preoperatively adequate enough to permit the hearing restoration to the 30 decibel level.

Practical hearing improvements obtained following fenestration in clinical otosclerosis with preoperative evidence of unimpaired cochlear nerve function were as a rule permanently maintained at the practical level when the newly created window remained permanently open. There exists no clinical evidence of secondary cochlear nerve changes in these cases. However, since secondary cochlear nerve changes have only rarely been observed in the non-operated ear of such patients, definite conclusions that the fenestration operation prevented secondary cochlear nerve changes in these cases cannot as yet be drawn.

Results following this surgery, when estimated on the basis of written replies to a posted questionnaire, are completely unreliable in a large number of instances. Many deafened people who are socially and economically insecure and do not like to call attention to their infirmity by wearing a hearing-aid, also hesitate to admit their deafened state in writing, though they would gladly admit it in confidential consultation with their physician.

Following a successfully performed fenestration operation in one ear, an improvement of hearing in the non-operated ear which could be audiometrically substantiated in more than one audiometric reading has never been observed.

CONCLUSION

The Lempert fenestra nov-ovalis technique, whereby the fenestra is created in the surgical dome of the vestibule, when carefully performed can result in the restoration and permanent maintenance of practical serviceable unaided hearing in a high enough

percentage of cases to render the surgical treatment of clinical otosclerosis acceptable to both the otologist and his patients.

There exists evidence now which suggests that the percentage of permanent practical hearing improvements is still further increased when the fenestra edges are treated with pure lead.

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DISCUSSION ON PRIMARY TREATMENT OF VARICOSE VEINS

Mr. A. Dickson Wright: Varicose veins have been the despair of surgeons ever since aseptic surgery began. Growing out of patience with a condition which recurs in the face of all treatments, surgeons have at times cast reason to the winds and performed most brutal and illogical operations. Rindfleisch-Friedel went to the extent of cutting the skin spiral wise from the knee to the ankle, and the resulting wound was left to heal by granulation. The healed legs resembled more those of a Chippendale table than a human being and gave endless trouble thereafter. Another vicious method was to circumcise the skin of the leg just below the knee down to the deep fascia, so that every superficial vein was divided. This did not help the varicose veins and sometimes ended in amputation from contraction of the scar. Extensive and laborious dissection of the veins was carried out by others and the results were poor. Mayo invented a ring stripper to strip out lengths of veins, and Babcock passed a long probe down the vein and tied it to the vein lower down, a large length of the vein was then dragged from its bed.

The injection treatment first thought of by Pravaz and elaborated by Sicard and Forestier provided an escape from the disappointing surgery of the day and seemed a subtle way out of the difficulty, but, after an enthusiastic start, the results proved disappointing, because of recurrence. An attempt was made to diminish the recanalization by using different sclerosing agents, but although some were better than others, the treatment proved inadequate, especially in those cases in which, owing to valvular defect, there was a free communication with the deep veins shown by the impulse on coughing, and various filling tests such as those of Trendelenburg, Perthes and Ochsner and Mahorner. It was then felt that a combination of surgery and injection treatment would be made in these advanced cases by ligaturing the saphenous veins at the femoral confluence and injecting sclerosing solution down the divided vein. Results were improved by this plan, but still there were recurrences and further ligatures were carried out just above the knee to cut off a deep communicating branch at this point, and also the short saphenous was tied in the popliteal space and occasionally a gluteal vein was tied. Dodd then suggested ligaturing the internal saphenous in front of the malleolus together with an upward injection of the divided vein. Even with all these ligatures some cases still recurred, because varicose veins, if patent, will draw blood into their commodious interiors from any source available and deep communicating branches, although important, did not provide the answer to all the problems. Once the veins refill, they will grow again and ramify without benefit of communicating veins; after all, they started long years before without this benefit. Driven by these failures to more radical measures, the out-patient treatment of the more severe cases could not be adhered to, and the cases were brought in so that a general anæsthetic could be given, and all the necessary ligatures carried out at one session, and, with the patient unconscious, a very thorough injection of the varicose veins carried out using a total quantity of 100 c.c. of 30% saline. The object of this is to endeavour to get every varix in the legs thrombosed and all deep communicating veins closed at the same time, so that the whole varicose network disappears at once, and the chance of recurrence is reduced to a minimum. Bandaging of the leg with elastoplast after these thorough procedures also helps greatly in reducing the bulk of the clots and helping to secure venous obliteration with the minimum of clot formation. One night in hospital suffices for all this, because it is important to get the patient out of bed as soon as possible. If any veins escape this

added that the operation was a great advance in surgery. This world-wide interest in fenestration was an excellent thing for surgery in general, but he hoped surgeons' researches would include the whole structure and function of the temporal bone.

Careful technique meant so much in this operation and some present, young as well as old, might find that they were not so equipped as to be able to do it. In that case they should be big enough to realize their limitations and not try. Others would fail to obtain results in this operation. They should stop for a while, and go to some of the masters to learn just that little bit more.

Dr. J. Lempert said that perhaps the best way he could answer Mr. Cawthorne's question about results would be as follows: If he were to take 100 patients and examine them and find them most suitable for the operation, if they were the type of patient whose hearing could be restored to the practicable decibel level for the three speech frequencies and higher, he could in this type of case restore practical, serviceable, unaided hearing in about 80 out of the 100. If then he waited two years and examined those 80 successful cases at the end of that time he would find himself left with only 60, the condition having recurred in the other 20. This meant that in 25% of the cases that were successfully operated on and in which hearing was restored, there was no longer practical hearing after two years. The other 75% would keep their hearing permanently. Such were the figures which had been obtained up to the present but with advances in technique, especially the new method of bone-dust-free fenestra technique, there might be an improvement. Only time would show whether this new technique resulted in a larger proportion of cases in which permanent hearing was restored.

He wished to say something about the patient who came to the otologist and wanted to have a fenestration operation and was found suitable for such operation. It was always best on finding such a patient to tell him the facts. He should be told that he was a suitable case for operation and what the chances of success were. It should be explained to him that there was an 80% possibility of restoring his hearing immediately and a 60% possibility of maintaining his hearing permanently. It should also be explained to the patient that there was perhaps one chance in 100 that the hearing would get worse instead of better in the operated ear following the operation. It should also be explained to him that he might well have vertigo for the first few days, that he would have to stay in bed for five days, remain in hospital for ten days and a week later he should be going about his own affairs.

As far as post-operative infection was concerned, he had tried many things to avoid this. The most satisfactory way of avoiding it was to get rapid healing, and to get rapid healing one had to do some skin grafting. With a good skin graft from the thigh, used immediately on the operating table, one should in three or four weeks have a dry and completely healed cavity. But there were cases which would stay dry for a while and then begin to desquamate and some mild staphylococcal infection would make its appearance. There was nothing he could tell them about that which they did not know already. In one case an excellent result would be obtained with sulphathiazole, but when one began to use it for other cases it did not seem to do the same amount of good. Another thing was a solution of gentian violet, and another was sulphadiazine and plain boric acid. In another case one might follow the bold plan of saying to the patient, "Do nothing, and don't see me again for three months", at the end of which time one may find the cavity completely healed. The worst thing one could use was silver nitrate. Some of these wounds continued to discharge for months or even for years. Others dried up perfectly within a relatively short time. He could only suggest that where one thing did not serve another should be tried.

Mr. Simson Hall had spoken of the border-line case. Dr. Lempert had a very strong feeling about these border-line cases. He would not say that they should not operate on them where there were some secondary nerve changes and there was still sufficient cochlear nerve function reservoir for the 512, 1,024 and 2,048 frequencies to improve their hearing, though not to the practical unaided level. However, anybody whose livelihood depended upon their hearing would not be satisfied with such a result. Such a person would still need a hearing-aid. Since an individual with inadequate cochlear nerve function cannot hear efficiently without a hearing-aid following fenestration, then he would suggest that they should keep their hearing-aid and not be operated on at all.

On the other hand, there were people who were economically secure and who refused to wear a hearing-aid for social intercourse and wanted to hear a baby cry or to follow conversation when playing bridge. For them the fenestration operation was justifiable and they could get a good enough result to be satisfied without wearing a hearing-aid. But the fact that they did not wear a hearing-aid should not lead to the supposition that they would not need such an aid to achieve economic and social security if they needed it. Over 80% of the deafened who came to see him wore hearing-aids but they were averse to using hearing-aids because they did not want to proclaim their infirmity. They did not want a "crutch". If they could get their hearing restored with the fenestration operation, that was what they wanted, even if there was inadequate bone conduction hearing in the high frequencies which would make the restoration of practical hearing doubtful. If they still wanted it even after a full explanation of what could be obtained by means of a hearing-aid and by means of operation respectively, there was no reason why they should be denied the operation. But these people could get only a limited improvement in hearing, which was not practical or serviceable enough for them to continue their life's work without the additional use of a hearing-aid.

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onslaught they must be followed up ruthlessly with injections of quinine, salicylate, ethamolin or P.G.3 solution (gelatine 0.5 gramme, dextrose 25 grammes, glycerin 30 grammes, phenol 2 grammes, aq. dest. to 100 c.c.).

There are signs of restiveness even with this treatment and a long blunt needle has been devised by Stevenson, so as to place the injection a long way down from the ligature in the groin; others recommend the ureteric catheter to achieve this. Riddoch goes even further in using a rasper passed down the vein so as to damage the intima at the time of the ligation and injection.

The contra-indications to treatment are old age, obesity, and diabetes. If arterial disease is present, great caution is indicated. If the patient has a history, family or particular, of easily provoked phlebitis, it is wise to abstain from treatment, because dangerous venous and even arterial thrombosis may occur in vital parts of the body if these patients are injected with sclerosing solutions.

The complications of treatment are important. If one has by chance stirred up a thrombophilia, then the case must be taken very seriously and anti-coagulants used to tolerance point, and if minor pulmonary embolism occurs, the femoral vein or veins should be tied.

Allergic manifestations are commoner with the fatty acid sclerosing agents and may be very severe and should be combated with adrenaline, ephedrine and benzedrine. The same agents occasionally produce most violent backaches, and even neck-aches and headaches shortly after injection, sometimes requiring intravenous morphia. Excessive inflammation of the veins is well managed with elastoplast bandage and necrosis is treated the same way. Femoral or posterior tibial thrombosis is generally due to keeping the patient in bed, or to thrombophilia.

The complications of varicose veins, thromboses, eczema, pruritus, and ulceration, are all cured by obliteration of the varicose veins except a hard core of cases with incompetent deep veins or old femoral thrombosis. These are treated by the various forms of compressive bandages and pads which are varied with the type of case and the sensitivity of the patient's skin. The main thing to remember is that every chronic ulcer of the leg will heal with adequate support (or rest in bed) except those due to specific infections such as syphilis, tropical spirochætal ulcer, Ducrey sores, mycosis and malignant disease.

Mr. J. B. Kinmonth: I propose to discuss the treatment of varicose veins in the light of information derived from venographic and histological studies. The X-ray studies comprised about 100 venograms made at operation and also on out-patients. The histological studies were made on portions of veins removed at operation from some 20 patients who had previously had their veins injected. Before dealing further with these investigations it is necessary to consider the theoretical basis of the various therapeutic injection techniques.

In every case a solution is injected which is damaging to living tissues, in order to cause the obliteration of the diseased vein. Inefficient circulatory channels containing stagnant or distal flowing blood are thus eliminated.

Methods fall into two groups according to whether the injected solution is fixed where injected, or passes on to be diluted in the general circulation.

(1) *Immediate clotting and fixation.*—The older method is injection into stationary blood behind a tourniquet which is removed when firm clotting has occurred. The clot is painful and bulky, and may involve deep veins as their blood flow also is impeded by the tourniquet. Lord Lister used this method but abandoned it for these reasons.

(2) *Delayed clotting.*—Here fluid is injected into a vein, injures the lining and then passes on into the general circulation where it is diluted. The damaged vein ultimately becomes filled with clot which in time organizes. If sufficient injury has been done to the vein, obliteration will be permanent; if not, recanalization will take place. It is difficult to believe that any vein which recanalizes in this way with the valves, intima and walls damaged can that remains long enough to produce irretrievable damage and then passes on to be diluted as quickly as possible.

Having dealt with these theoretical considerations, it is now proposed to see what light venographic and histological studies throw upon current practice.

VENOGRAPHY

Injections imitating therapeutic injections were made with radiopaque dyes. Observations of three types were made:

(1) *Retrograde injection at operation.*—The rationale of this type of injection is to obliterate the great saphenous vein and possibly calf varicosities by injecting sclerosing fluid down a catheter passed from an incision in the groin. A series of venograms were made at operations injecting amounts varying from $1\frac{1}{2}$ to 8 c.c. of dye.

The venograms suggest this to be an inefficient method because: (a) Much of the dye goes straight into the deep veins. (b) Spasm of the great saphenous vein occurs due to irritation by the catheter so that little injected fluid stays in the vein. (c) Little fluid goes below the knee—it tends to pass into communicating veins or even normal veins.

With larger quantities of fluid than 8 c.c. the excess goes straight into the deep veins.

(2) *Fluoroscopic screening*.—Dye injected into normal superficial leg veins never passes distally—even if there is a tourniquet above the site of the injection. Dye injected into varicose veins with the patient standing sinks rapidly towards the ankle. Dye injected into a varicose vein with the patient lying remains at the site of injection until the patient moves the limb.

(3) *Serial venograms of direct injections into leg varicosities*.—These show that 1 to 1½ c.c. is the optimum amount for a single injection. Larger amounts tend to spill over into the deep veins. Entry to the deep veins is particularly likely to occur, as would be expected, in tributaries of the small saphenous vein at the back of the calf.

Serial pictures of the same injection confirm what was found on screening, that injections made into a vein with the limb horizontal and at rest remain stationary until the limb is moved.

The serial pictures also show that fluid passing into the deep veins remains there longer than one would expect: it is not swept instantly away but may often be seen still lying in some concentration a minute or more after injection. It remains for a longer time still in the communicating veins and can often be seen to linger in the neighbourhood of valves. As the valves are extremely delicate and vulnerable structures this is a very significant observation.

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Histological studies.—Small portions of vein were excised at operation from patients who had had injections of sclerosing fluid a few days beforehand. These injections were often inadequate clinical "takes" followed by no palpable clotting and little or no tenderness. And yet when the vein was removed it was found to show surprising changes both to the naked eye, when oedema of the walls and quite unsuspected clotting was observed, and also on microscopy. These changes were most marked in this region of the valves which were found on microscopy to be damaged and involved in adherent clot even when there had been no clinical "take".

CONCLUSIONS AS TO TREATMENT

(1) For more severe cases with incompetent great saphenous valves requiring operation: High saphenofemoral ligature probably combined with ligature at knee level or in the thigh if a communicating vein "blow-out" is detected. No retrograde injection. Local injection of calf varicosities if necessary at a later date.

(2) For mild cases: Injection of the affected veins using an empty vein technique with the limb horizontal. Not more than 1½ c.c. in each injection. The leg to be kept still for five minutes, then moved vigorously to sweep the fluid away.

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There are signs of restiveness even with this treatment and a long blunt needle has been devised by Stevenson, so as to place the injection a long way down from the ligature in the groin; others recommend the ureteric catheter to achieve this. Riddoch goes even further in using a rasper passed down the vein so as to damage the intima at the time of the ligation and injection.

The contra-indications to treatment are old age, obesity, and diabetes. If arterial disease is present, great caution is indicated. If the patient has a history, family or particular, of easily provoked phlebitis, it is wise to abstain from treatment, because dangerous venous and even arterial thrombosis may occur in vital parts of the body if these patients are injected with sclerosing solutions.

The complications of treatment are important. If one has by chance stirred up a thrombophilia, then the case must be taken very seriously and anti-coagulants used to tolerance point, and if minor pulmonary embolism occurs, the femoral vein or veins should be tied.

Allergic manifestations are commoner with the fatty acid sclerosing agents and may be very severe and should be combated with adrenaline, ephedrine and benzedrine. The same agents occasionally produce most violent backaches, and even neck-aches and headaches shortly after injection, sometimes requiring intravenous morphia. Excessive inflammation of the veins is well managed with elastoplast bandage and necrosis is treated the same way. Femoral or posterior tibial thrombosis is generally due to keeping the patient in bed, or to thrombophilia.

The complications of varicose veins, thromboses, eczema, pruritus, and ulceration, are all cured by obliteration of the varicose veins except a hard core of cases with incompetent deep veins or old femoral thrombosis. These are treated by the various forms of compressive bandages and pads which are varied with the type of case and the sensitivity of the patient's skin. The main thing to remember is that every chronic ulcer of the leg will heal with adequate support (or rest in bed) except those due to specific infections such as syphilis, tropical spirochaetal ulcer, Ducrey sores, mycosis and malignant disease.

Mr. J. B. Kinmonth: I propose to discuss the treatment of varicose veins in the light of information derived from venographic and histological studies. The X-ray studies comprised about 100 venograms made at operation and also on out-patients. The histological studies were made on portions of veins removed at operation from some 20 patients who had previously had their veins injected. Before dealing further with these investigations it is necessary to consider the theoretical basis of the various therapeutic injection techniques.

In every case a solution is injected which is damaging to living tissues, in order to cause the obliteration of the diseased vein. Inefficient circulatory channels containing stagnant or distal flowing blood are thus eliminated.

Methods fall into two groups according to whether the injected solution is fixed where injected, or passes on to be diluted in the general circulation.

(1) *Immediate clotting and fixation.*—The older method is injection into stationary blood behind a tourniquet which is removed when firm clotting has occurred. The clot is painful and bulky, and may involve deep veins as their blood flow also is impeded by the tourniquet. Lord Lister used this method but abandoned it for these reasons.

(2) *Delayed clotting.*—Here fluid is injected into a vein, injures the lining and then passes on into the general circulation where it is diluted. The damaged vein ultimately becomes filled with clot which in time organizes. If sufficient injury has been done to the vein, obliteration will be permanent; if not, recanalization will take place. It is difficult to believe that any vein which recanalizes in this way with the valves, intima and walls damaged can that remains long enough to produce irretrievable damage and then passes on to be diluted as quickly as possible.

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Injections imitating therapeutic injections were made with radiopaque dyes. Observations of three types were made:

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The venograms suggest this to be an inefficient method because: (a) Much of the dye goes straight into the deep veins. (b) Spasm of the great saphenous vein occurs due to irritation by the catheter so that little injected fluid stays in the vein. (c) Little fluid goes below the knee—it tends to pass into communicating veins or even normal veins.

With larger quantities of fluid than 8 c.c. the excess goes straight into the deep veins.

(2) *Fluoroscopic screening*.—Dye injected into normal superficial leg veins never passes distally—even if there is a tourniquet above the site of the injection. Dye injected into varicose veins with the patient standing sinks rapidly towards the ankle. Dye injected into a varicose vein with the patient lying remains at the site of injection until the patient moves the limb.

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TREATMENT OF VARICOSE VEINS

The sheet-anchor of treatment is ligation. In addition to proximal ligation where the main superficial vein enters the deep vein, distal ligations at the sites of incompetent perforating veins should be undertaken.

Internal saphenous system.—(1) *Proximal ligation of internal saphenous vein in the groin.*—The technique of the operation is well known. There are, however, a few points which I should like to stress.

(a) *Ligation of all the tributaries of the saphenous vein in the groin:* Reimann *et al.* (1946) have drawn attention to the common variations of the anatomy of the tributaries entering



FIG. 2.



FIG. 3.

FIG. 2.—Venogram showing well-marked deep phlebitis of calf. Patient, who had varices of internal saphenous vein below the knee, complained of aching pain in calf of leg.

FIG. 3.—Venogram of a patient with oedema of leg, showing deep varices affecting the posterior tibial group of veins.

the internal saphenous vein in the groin. Knowledge of these abnormalities is of no great surgical importance because every tributary entering the saphenous vein in the neighbourhood of the fossa ovalis should be ligatured and divided.

There is one, however, to which little attention has been paid and which may be missed. The accessory saphenous vein (either the medial or lateral superficial femoral veins may qualify by their size for assumption of the title of accessory internal saphenous vein) usually joins the internal saphenous vein within two or three inches of the sapheno-femoral junction. Sometimes, however, the accessory saphenous vein pierces the deep fascia 4 or 5 in. (10–12.5 cm.) below the fossa ovalis and runs upwards lying superficial to the femoral vein and joining the internal saphenous *deep* to the fossa ovalis (fig. 4A, B).

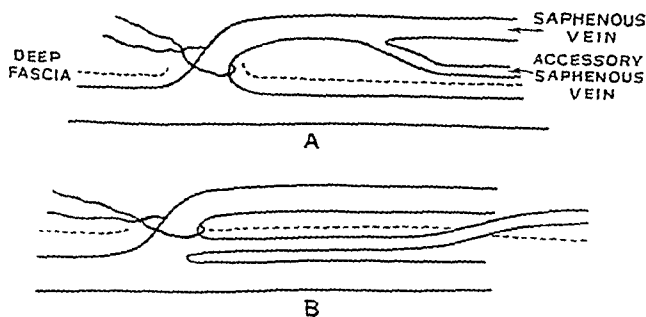


FIG. 4.—(A) Accessory saphenous vein joining internal saphenous vein 2 in. distal to fossa ovalis. (B) Accessory saphenous vein piercing the deep fascia 4 or 5 in. below fossa ovalis and joining internal saphenous vein in fossa ovalis.

since the time of Hippocrates. Before Lister's work failure was largely due to sepsis. Since it has been possible to operate aseptically, failure to obtain 100% successful results has led to the introduction of numerous combinations of operative and non-operative methods. One of the great handicaps in the assessment of the best treatment for varicose veins is the paucity of publications of end-results of cases accurately followed up. Ochsner in 1939 reviewed all the end-results published prior to that year. I have examined the follow-up results published since 1939. The recurrence rate after one year varies from 20-98%. Moore and Knapp state that after one year there is little change in the comparative results. That has not been my experience. 60 cases treated in the wards of the Surgical Unit at St. Bartholomew's Hospital were followed up by Alan Walker over a period of eight years. There was a steady increase in the recurrence rate year by year. The reason for these unsatisfactory results lies in the ætiology of varicose veins. I believe that varicose veins are primarily due to a congenital deficiency or weakness of the valves. The condition is progressive. No single operation is likely to cure them.

SYMPTOMS OF VARICOSE VEINS

Causes of pain.—(1) Varices of external saphenous system. (2) Complete dilatation of internal saphenous vein with saphena varix. (3) Involvement of cutaneous nerves in periphlebitis. (4) Deep phlebitis of the calf.

(1) *Varices of external saphenous system.*—Varices on the back of the calf are undoubtedly painful. The superficial and deep veins in the back of the leg do not communicate directly but via the muscular veins. Incompetency of the valves in these veins leads to varices in the calf muscles, the subcutaneous varices appearing later. It is these muscular varices which give rise to the aching pain of which patients complain.

(2) *Complete dilatation of the internal saphenous vein with saphena varix.*—This condition is due to deficiency or even absence of the femoral valve. Back pressure soon overcomes the resistance of the valves in the internal saphenous vein. Hence there is an unbroken column of blood from the right atrium to the ankle. This condition undoubtedly gives rise to discomfort—aching and a "heavy" feeling in the leg on prolonged standing (fig. 1A, B).

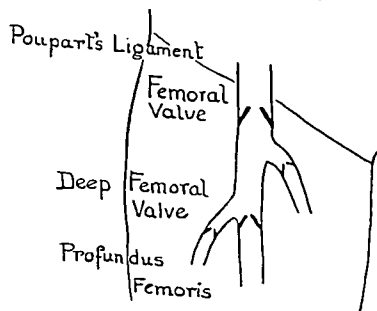


FIG. 1A.

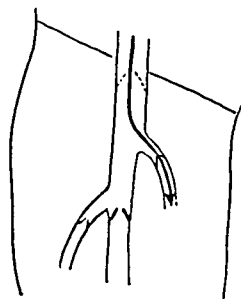


FIG. 1B.

FIG. 1.—(A) Diagram of valves, groin region. (B) Illustrates effect of back pressure on saphenous vein when femoral valve is weak or absent.

(3) *Involvement of cutaneous nerves in periphlebitis*—usually the saphenous—by inflammatory changes round varices, particularly "blow-outs", gives rise to paroxysms of intense burning pain.

(4) *Deep phlebitis of the calf.*—Dr. R. N. Tattersall drew my attention to the frequency of deep phlebitis in patients with varicose veins who complain of calf pain. I fully concur with his view. Venograms of patients with internal saphenous varices below the knee who have genuine pain in the leg show varying degrees of deep phlebitis. The presence of deep phlebitis should always be suspected if a patient with incomplete internal saphenous varices complains of aching pain in the calf on standing, especially if there is any œdema of the ankle (fig. 2).

Deep phlebitis is *not* a contra-indication to ablation of the superficial varices; it is in fact an indication for operative treatment.

œdema due to chronic venous insufficiency.—Venographic examination of chronic œdematous legs with or without superficial varices has occasionally shown gross varicosities of the deep veins. This seems to me to be of great importance explaining chronic swelling of a leg in which there is no history of phlebitis. Moreover it explains the success of ligation of the femoral vein in occasional cases diagnosed as thrombophlebitis (fig. 3).

were carried out at both groin and knee levels. In every case where injection was given in the groin, the solution passed into the femoral vein through the perforating vein in the

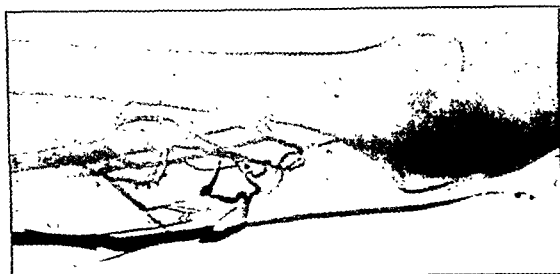


FIG. 7.—Ven ogram showing filling of femoral and upper third of popliteal vein following injection of pyelectan into distal end of divided saphenous vein.



FIG. 8.—Saphenous vein divided just below the knee. Pyelectan injected into distal end. Some opaque solution has passed through a perforating vein just below the knee filling the popliteal vein.

lower third of the thigh. Plates exposed one minute later showed the opaque solution in the femoral vein. A further skiagram ten minutes after injection, when the superficial veins were firmly sclerosed, showed the radiopaque sclerosant still present in the femoral vein (figs. 9 and 10).

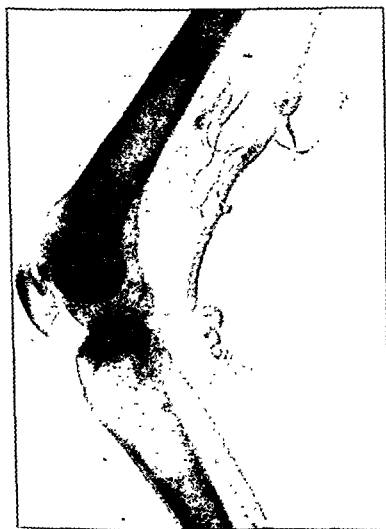


FIG. 9.—Venogram showing radiopaque sclerosing solution in femoral vein following injection of the solution into distal end of divided saphenous vein.



FIG. 10.—Venogram of same patient taken ten minutes later showing radiopaque sclerosant still in femoral vein. Superficial veins were firmly sclerosed.

Injection from knee level produced results similar to those obtained from pyelectan. Unless there happens to be a perforating vein of unusual size very little of the sclerosant will enter the deep vein.

These observations prove beyond doubt that retrograde injection of sclerosing solutions are unsafe, at all events if the injection is given at groin level. Probably small injections of

It is extremely easy to mistake the accessory saphenous for the femoral vein, ligating the saphenous vein *distal* to the entrance of this large tributary instead of at the sapheno-femoral junction. The result is *complete* failure to prevent filling of the varicosities. Fig. 5 shows a venogram of a case in which this error has been made.

(b) *Ligation of saphenous veins flush with the femoral vein*: Much unnecessary emphasis is, in my opinion, placed on the necessity of ligating the saphenous vein flush with the femoral vein. The concept of clot forming in the stump of the vein and giving rise to pulmonary embolism seems to me highly theoretical. The necessity for a similar procedure has never been stressed in ligation of large tributaries of other main veins—for example, ligation of the distal end of the internal jugular in block dissection of the neck, or the external jugular in other incisions in the cervical region, or the subscapular vein in radical mastectomy.



FIG. 5.—Venogram of patient after ligation in groin in which ligature was placed distal to entrance of accessory saphenous vein instead of at the sapheno-femoral junction.

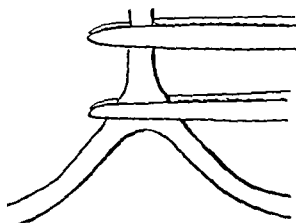


FIG. 6.—Method of injury of femoral vein in flush ligation at sapheno-femoral junction.

These observations have been criticized on the grounds that, while a non-irritant solution entered the deep veins, a sclerosing solution would either thrombose the perforating veins so rapidly or cause such spasm that leakage into the deep vein was improbable. Alternatively, if any did reach the deep veins it would be diluted and swept away so rapidly that no damage to the deep veins was likely to occur.

My Lecturer, Mr. John Loewenthal, suggested to me that these points could be cleared up by using a radiopaque sclerosant. All the common sclerosing solutions were mixed with the various radiopaque organic iodine solutions in varying proportions without success. Mr. J. B. Lloyd, M.P.S., Chief Pharmacist to the Manchester Royal Infirmary, solved this problem for us with the following solution: Sodium ortho-iodohippurate 75%; mono-ethanolamine oleate 5%; benzyl alcohol 2%. This is both an excellent sclerosant and of adequate radiopacity. The iodine is absorbed within an hour.

Retrograde injection with radiopaque solution.—Retrograde injections of this solution

I would go further—I believe it is undesirable. It is extremely easy to injure the femoral vein in a similar way to the classic injury of the common bile duct, by deforming the sapheno-femoral junction by traction on the proximal end of the saphenous vein in an attempt to define the exact point of union (fig. 6).

(2) *Distal ligation.*—(a) *Lower third of thigh*: A short segment of the internal saphenous vein including the perforating vein should be excised. The exact site can be found by means of the tourniquet test of Mahorner.

(b) The communicating vein often found behind the knee between the external and internal saphenous veins should be ligated if present. This is best carried out through a vertical incision in the popliteal fossa, so that proximal ligation of the external saphenous vein can be done at the same time if required.

Injection of sclerosing substances.—*Dangers of retrograde injection*: Deep phlebitis occasionally follows retrograde injection of sclerosing solutions. Retrograde injection of pylectan into the distal end of the saphenous vein divided in the groin has been shown by X-ray to enter the femoral vein via the perforating veins in every case in which it was used (fig. 7).

If the retrograde injection is carried out from knee level, the radiopaque solution could only occasionally be seen in any quantity in the popliteal vein.

As a rule the capacity of the superficial varicosities was so great that all the solution was taken up by them, negligible quantities leaking into the deep veins through the perforating branches. Occasionally, however, the perforating veins, especially the highest situated at the level of the lower border of the head of the tibia, are very large, allowing most of the solution to enter the popliteal vein (fig. 8).

sclerosants, as Mr. Kinmonth had shown, provided the answer to the disrepute of such varicose vein therapy; the patient was often saddled with the added serious disability of deep vein damage.

Mr. A. S. Till asked whether the ligation of painful varicose veins was countenanced during pregnancy.

In these days it was generally not possible for pregnant women to rest for long periods and in several such cases in second or subsequent pregnancies ligation had been carried out with marked relief.

Mr. R. H. Gardiner asked if the hæmaturia which occasionally occurred after the injection of sclerosing agents into the internal saphenous veins in the groin might be explained by the rapid absorption of these agents into the general circulation, in view of what had been shown by the venograms seen earlier in the discussion. He thought it possible that certain agents might have a toxic effect on the parenchymatous organs, particularly the kidneys. In his experience, injection of sclerosing agents at the groin level was not necessary, as adequate clotting appeared to take place in the internal saphenous veins in the thighs if the veins were ligated in the groin and again just above the level of the knee-joint.

Professor Boyd (in reply) agreed with Mr. Cohen that deep phlebitis was not necessarily a contra-indication to treatment of the superficial varices. Chronic venous insufficiency of the superficial veins required treatment on its own merits and should be considered separately from deep venous insufficiency. The view that superficial varicosities are "compensatory" due to deep obstruction is erroneous. As Turner Warwick has shown, deep obstruction will not cause reversal of flow in the deep perforating veins unless there is a congenital weakness or deficiency of the valves in the perforating veins, i.e. unless the patient is of a varicose tendency and would have developed them anyhow. Dilatation of superficial veins in obstruction of the femoral veins or even of the inferior vena cava are the exception rather than the rule. He did not feel, however, so certain about the value of high femoral ligation in deep phlebitis. Femoral ligation only occasionally results in dramatic relief of oedema in "deep phlebitis". It is probable that in the successful cases of femoral ligation the oedema was, in fact, due to varices of the deep veins (see fig. 3) rather than to deep phlebitis.

Professor Boyd was extremely interested in Mr. A. S. Till's question about the desirability of ligation of varicose veins during pregnancy. He had had no experience in the treatment of varicose veins during pregnancy but saw no contra-indication to ligation, should the veins be a source of discomfort.

He agreed with Mr. Gardiner that hæmaturia following injection of varicose veins was probably due to rapid absorption into the general circulation and renal damage. He recalled seeing hæmaturia following injection of sclerosants on several occasions during the war but could not remember whether quinine-urethane or sodium morrhuate had been used as the sclerosing agent. He was inclined to think that the quinine solution had been used.

[May 5, 1948]

DISCUSSION ON VAGAL RESECTION FOR PEPTIC ULCER

Mr. Ian Orr: It would be impossible, in this brief Address, to refer in detail to the rapidly accumulating literature on vagal resection, or to describe the results of numerous animal experiments designed to determine the secretory changes found in vagotomized animals.

I shall confine my remarks to describing the rationale, the mode of investigation and findings in a series of 115 vagal resection operations performed by Mr. H. D. Johnson and myself at Hammersmith and other hospitals.

Rationale.—The rationale is based on the present medical conception of ulcer therapy; namely, that in the control of acid secretion continuously throughout the twenty-four hours lies the key to healing.

When the physician treats a patient with duodenal ulcer, he aims at providing mental as well as physical rest by withdrawing the patient from his environment, excluding him from domestic and business worries, and thereby reducing the intensity of the cephalic stimuli travelling to the stomach by way of the vagi. He supplements this mental rest by large doses of atropine, which, acting on the endings of the vagus, relaxes the pylorospasm commonly found in the duodenal ulcer patient, and inhibits both the motility and secretory activity of the stomach. According to Douthwaite the dose of atropine requisite for this purpose has to be sufficient to produce toxic manifestations. Even this is insufficient to cut down the acid in the vagotonic patient to a level compatible with healing of the ulcer, and the residue of acid has to be buffered by a continuous milk drip. The importance of continuing this buffering effect throughout the twenty-four hours is now fully appreciated. That medical

not more than 3 to 5 c.c. at knee level are in most cases quite safe. How frequently the highest calf perforating vein is large enough to allow the solution to enter the popliteal vein has yet to be determined. The saphenous vein should be exposed and the retrograde injection given about 1 in. (2.5 cm.) below the head of the tibia in order to be certain of being below the highest perforator.

CONCLUSION

I wish to stress the congenital basis and progressive nature of varicose veins. Operation should only be advised if there is definite evidence of chronic venous insufficiency or for genuine pain or discomfort. Operation for purely cosmetic reasons should be discouraged. Treatment should consist of ligation of the internal saphenous vein in the groin; excision of a segment including the perforating vein in the lower third of the thigh; excision of another segment including the perforating vein immediately below the knee if this is found to be large; retrograde injection from knee level of 3 to 5 c.c. of sclerosant solution. The communicating vein behind the knee, if present, and sometimes the external saphenous vein, should be ligated if there is valvular incompetence.

Compression of the vein walls to avoid painful and unsightly thrombosed veins is secured by an elastoplast bandage applied firmly and evenly from *above downward* beginning a few inches above the point of injection and continued as far as the metatarsophalangeal joints. The patient is confined to bed, the foot of which is raised on 5-in. blocks, for one week.

I have only seen one example of pulmonary embolism following operation for varicose veins. This was in a woman of 50 who had a small pulmonary infarction; she had been operated upon as an out-patient under local anaesthesia and treated by immediate ambulation.

In my opinion the groin wound heals better and the cosmetic result is improved by confining the patient to bed.

Finally I should like to pay a tribute to the pioneer work of Turner Warwick, whose delightful monograph published in 1931 contains almost all the observations which have since been made.

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Mr. Peter Martin advocated the importance of constant and firm pressure on long-standing varicose ulcers and said that in his experience the best method of applying this pressure was by a two-way stretch non-adhesive bandage.

Mr. Sol. M. Cohen questioned whether deep venous thrombosis should be regarded as a complete contra-indication to any form of operation. These were the patients particularly liable to serious limb sequelae, and surgery had hitherto but little to offer. The clot and phlebitis fixed and impeded vein valve action, and as the lumen was only partially filled by clot, blood "snaked down" from the vena cava, subjecting the distal venous tree to the full gravitational force of a long column of blood. High femoral vein interruption was thus a rational procedure, and he had practised such deliberate ligation in some of these cases, with beneficial result. He was opposed to sclerosant injection coincident with the operation; the rapidity with which such injected material entered the deep circulation could be demonstrated readily by injecting pentothal into a varicosity—the onset of general anaesthesia being found to be very little delayed. The *fons et origo* of the post-operative embolus was the thrombosis in the deep veins secondary to sclerosant diffusion, and not, as commonly taught, clot formation clinging perilously to the saphenous vein stump. Sclerosant injection was particularly hazardous under general anaesthesia; for with flaccid limb there was pooling and stagnation within the deep veins. Multiple vein resection operations, although tedious, yielded gratifying results. Professor Boyd had explained in lucid fashion the probable mechanism of pain with such varices, and provided an explanation for the completely symptom-free clinical picture, in spite of the presence of gross varicosities. The latter were not, however, to be regarded as benign and inconsequential for, besides the remote effects on the general circulation, there was as yet no true explanation of the factors underlying the development of varicose ulceration. Varices were a frequently associated feature, but the lesion was ischaemic on microscopy; the arterioles in the area were found to be compressed or strangled by the fibrous tissue reaction secondary to lymph fluid seepage and stagnation. The frail nature of the vein valves and their ready damage by

Polya type of anastomosis. This antrectomy, plus vagotomy, has resulted in the most marked fall in acid, as the hormone as well as the nervous secreted acid has been dealt with and gastric drainage has been adequate. Some of our most spectacular results have been in this antrectomy plus vagotomy group.

Methods of investigation.—For the proper selection of cases a routine investigation is essential. The barium meal study, in addition to determining the existence of an ulcer, should indicate the rate of emptying, the possibility of minor degrees of stenosis and the absence of other pathology such as duodenal diverticula or gastric ulcers which might confuse the result.

The acid secretion tests are of great importance and though the standard fractional test meals are carried out in many of the cases, the finding of greatest importance is the quantity and acid level of night secretion entirely unstimulated by food, or drugs. This entails continuous gastric suction throughout the night, titration of hourly samples and estimation of the total quantity of free acid secreted. It is on the basis of this estimation that the decision to resect the vagus is made.

The insulin test meal is also employed both before, and on several occasions following, operation. Its main value lies in providing an indication whether or not the vagotomy has been complete. Sufficient insulin is given intravenously to produce a fall in the blood-sugar level to 50 mg. per 100 c.c., or lower. This degree of hypoglycæmia leads to a stimulation of the hypothalamus which, acting through the vagus nerves, results in a marked outpouring of gastric juice. If even one fibre of the vagus is left intact this response may be obtained. A comparison of the insulin response before and after operation therefore provides a reliable, but not infallible, indication of the completeness of the operation.

The operative technique was then demonstrated by means of coloured illustrations.

Post-operative régime.—Even the best vagal resection may lead to the most unfortunate results if the importance of the early post-operative management is left to the discretion of ward sisters and house surgeons. It is essential to decompress the stomach completely for five days after the vagotomy. This was not appreciated in our earlier cases and some of those who had troublesome retention might have enjoyed a much greater benefit by an earlier application of this principle. Some of the very unsatisfactory cases recently reported in American literature also appear to have been due to neglect in this respect. The patient is given only intravenous feeding for five days, and food and water by the mouth are entirely withheld. When the tube is removed the patient is given fluids, one ounce per hour, and the stomach tube is passed in the evening and the gastric contents aspirated. If the day's ration of fluid appears to have passed successfully, two ounces hourly are allowed the next day. If this passes successfully he is placed on a liquid diet with instructions to cease drinking if he feels distended. A few days later, if the liquid diet is passing the pylorus, semi-solid food is added and gradually the diet is built up. It should be possible to allow a full normal meal in a month from the date of the operation. Given rest, Auerbach's plexus establishes an autonomous motility which may reach a degree of activity equal to normal.

These cases are allowed to sit and stand up forty-eight hours after operation, unless there is some other counter-indication, and by the end of a week they are surprisingly active.

Results.—Post-operative follow-up is made of all cases. They are readmitted as bed space permits for a repeat of their night secretion tests, and barium meal studies, after three months have elapsed. Tests performed soon after the operation may be misleading due to delayed emptying of the stomach and other factors. The patients are seen again at six-monthly intervals for two years, and then once a year with instructions to report immediately any untoward event. 115 operations have been performed (Tables I and II).

TABLE I.—TOTAL CASES, 115

Believed to be complete	88
Believed to be incomplete	27
Vagal resection alone	96
Vagal resection plus gastro-enterostomy	10
Vagal resection plus gastrectomy	9
Transabdominal approach	111
Trans thoracic approach	4

TABLE II.—96 PATIENTS FOLLOWED UP REGULARLY SINCE OPERATION. CASES UNDER THREE MONTHS EXCLUDED

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SEPT.—SURG. 2.

therapy heals a high proportion of duodenal ulcers there is no doubt whatever. Unfortunately when these people return to their normal activities the cephalic stimuli return with their former intensity and it is no longer possible to anchor the patient to his milk drip or continue to push atropine to the limits of tolerance, and within two years a regrettably high percentage of these ulcers recur.

Present-day surgical therapy also depends for its success on the control of acid, and it has been found necessary to remove the greater part of the acid-secreting portion of the stomach to protect the jejunum used in the anastomosis. Both physician and surgeon aim at the control of acid, one by the exhibition of therapeutic measures over a limited period, the other by ablating the organ which secretes the acid. Much confusion of thought would be avoided if it were clearly recognized that acid may be secreted in response to two entirely different types of stimuli. One is due to a hormone, believed to be formed in the first part of the duodenum and the pyloric antrum. In normal people this is the predominant factor in acid secretion, and as it occurs only when there is food in the stomach to buffer it, its action is entirely beneficial. On the other hand recent work by Johnson has shown that a large and unfortunately growing class of people secrete acid in response to nervous stimuli. This secretion is not limited to psychic stimuli such as the sight, smell and taste of food, but is continuous throughout the hours of sleep; and in fact it may reach higher levels while the stomach is empty than it does following a test meal. If we remember this we see how important it is for the physician to treat the patient by a continuous milk drip during the hours of sleep, and how essential it is for the surgeon to remove all the secreting part of the stomach if he is to avoid the danger of a stomal ulcer. But if this acid, secreted in response to nervous stimuli, is as important as recent investigation would suggest, it is at least rational to attempt to eliminate it by interrupting the nerve pathways. This, then, is the rationale of vagus resection. If it can be shown that the quantity of acid secreted during the hours of sleep is appreciably reduced, that the hypermotility and pylorospasm are abolished, that pain is relieved and the ulcer shown to heal, then, indeed, we have a humane experiment worth following up in all its aspects. If, in addition, our follow-up shows a persistence of the benefits and a lack of disabling side-effects, we have contributed something of permanent value in the therapy of duodenal ulcer. Even though it is unlikely to supplant medical treatment or gastrectomy entirely, a place may be found for it among the accepted procedures of our time.

Anatomical considerations.—The right and left vagus nerves distribute themselves in the form of a plexus around the œsophagus below the hila of the lungs. On the lower two inches of the œsophagus, however, the multiple branches group themselves into two to four main trunks, related to the anterior and posterior aspects of the œsophagus, and it is at this point that they are most easily located and followed through the hiatus and a segment resected. The approach favoured by Allen is transthoracic, on the assumption that only by this route can the vagotomy be made complete. Dragstedt, who has performed four hundred vagal resection operations in the past five years, began with the thoracic approach but of recent years has adopted the transabdominal route. At Hammersmith we have employed a trans-abdominal, trans-hiatal approach in all but four of our cases, and with growing experience complete vagotomy has been achieved, though in many of the early cases fibres were missed and the results were disappointing. The advantage of the transabdominal approach is that the ulcer can be seen and verified, other pathology detected, and additional operative procedures carried out if thought necessary.

Selection of cases.—The ideal case for vagal resection alone is the patient with a duodenal ulcer with a rapidly emptying stomach and a highly acid night secretion. Gastric ulcers are, in our experience, unsuitable for treatment by vagal resection alone, though Dragstedt finds it beneficial; and Professor Beattie, in his recent Hunterian lecture, looks upon it as an indication. We have rarely found the gastric ulcer case with a night secretion sufficiently high to justify a vagotomy, and we agree with Allen that in view of the risks of malignancy, if surgery is indicated at all, such ulcers are better resected.

Stomal ulcers following gastrectomy provide a first-class indication for vagotomy. Indeed, it may be the only surgical procedure practicable. Stomal ulcers following gastro-enterostomy appear to do well on vagal resection alone, but on theoretical grounds it seems rational to remove the pyloric antrum at the same time, thereby eliminating hormone-secreted acid as well as the acid under nervous control.

Ulcers complicated by stenosis, even relative stenosis, do badly with vagotomy alone in view of the fact that gastric motility is reduced and gross gastric retention is likely to follow. In the earlier cases in the series, we performed a posterior gastro-enterostomy at the same time as the vagotomy, or as a secondary procedure if gastric retention became manifest later. The results (some of them three years old) have remained good to date, but during the past year we have resected the pyloric antrum at the time of the vagotomy operation, employing a

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Over 1 year	1	1	1	14	4	1 (G.U.)
Under 1 year	6	2	1	34	7	1

72 patients have expressed themselves well satisfied with the operation.

15 are partially satisfied.

Only 2 patients out of 69 in whom vagal resection has been shown to be complete have had a continuation or recurrence of symptoms.

To date there have been no deaths due to vagotomy, though one of our early incomplete cases sustained a severe hæmorrhage three months after vagotomy, from which he died; and another had a duodenal fistula due to the resection of a penetrating ulcer, following an uneventful vagotomy. He subsequently died from an attempt to close the fistula.

One patient who had been symptom-free for a year with a negative insulin response and persisting low acid, had a hæmatemesis. Complete investigation failed to detect a recurrence of the ulcer, and the final conclusion was that he bled from œsophageal varices.

One patient with both gastric and duodenal ulcer at the time of the original operation continued to suffer from pain, due to the gastric ulcer. This experience has tended to damp our enthusiasm for vagal resection in the treatment of gastric ulcer.

The earlier attempts to resect the vagus nearly always resulted in missing an important branch, with the result that the effect was transient. One fibre appears to be capable of transmitting the total vagal impulse and considerable experience is necessary before the operator can be sure of the completeness of his operation. Most of the unsatisfactory results in this series have been found in the incomplete group.

Complications.—Of the immediate post-operative complications, basal collapse has been the most frequent, and occurred in 50% of the cases. In no case did it give rise to anxiety. Two patients had burst abdomens due to post-operative coughing. No case of pulmonary embolism has been noted and, due to the post-operative decompression of the stomach, there has been no case of acute dilatation of the stomach or complete gastric retention, though these disasters have featured in at least one of the series reported from America (Tables III and IV).

TABLE III.—IMMEDIATE POST-OPERATIVE COMPLICATIONS

Respiratory, not serious	56
Empyema following transthoracic operation	1
Acute dilatation of stomach	0
Burst abdomen	2

TABLE IV.—LATE POST-OPERATIVE COMPLICATIONS

Gastric retention, not associated with stenosis, requiring surgery for relief	0
Gastric retention, associated with organic stenosis, requiring surgery for relief	6
Gastric retention relieved by aspiration or recovering spontaneously	5
Diarrhœa: Transient and not incapacitating	56
Persistent	1
Dysphagia: Transient	8
Persistent	1
Attacks of weakness and giddiness	28

The late complications have, for the most part, been transient and tended to rectify themselves spontaneously. A feeling of fullness after meals and belching is common in the first six months. Diarrhœa has been troublesome in 50% of cases. This tends to clear up, but may recur from time to time following chills, indiscretions in diet, &c. Two complaints are of interest, not so much from their disabling effects as from the questions they raise regarding their cause. Slight difficulty in swallowing has been noted in 9 patients, and 28 have admitted on questioning to experiencing transient attacks of weakness and sweating, passing off when something is eaten. Most of those 28 patients volunteered the statement that such sweating attacks closely resembled the upset they experienced after intravenous insulin.

Conclusion.—No attempt will be made at this stage to compare the results of vagotomy with gastrectomy. The operation of vagal resection alone carries no mortality other than the risk of an odd fatality which is bound to occur in any large series of operations. Where it is combined with a gastrectomy or gastro-enterostomy, of course, it carries the risk of the major procedure. The economic factor in time lost from work weighs heavily in favour of the vagal resection, and the post-operative complications and disabilities, whilst by no means negligible, are not of an incapacitating order.

The follow-up statistics present a more gloomy picture than the faces of the patients who attend the follow-up clinic. The symptoms recorded are mostly obtained by close questioning; and the voluntary statements of the vast majority of those in whom the vagotomy has been complete are emphatic in their gratitude for the relief afforded after years of invalidism and repeated courses of medical treatment.

We know now that vagal resection is capable of lowering free acid levels to a marked degree, and that pain is relieved, and ulcers heal. Its final usefulness may be as an adjuvant to other

gastric procedures. We may find ways and means of avoiding the unpleasant side-effects and rendering the completeness more certain.

To be worth doing at all vagal resection must be complete, the patients must be carefully chosen and the post-operative régime must be strict.

There are precise indications for the operation and it should not be resorted to as a way out when one is doubtful about the diagnosis or apprehensive about more radical procedures.

This report on the first hundred and fifteen cases has dealt mainly with vagal resection alone, but the excellent results obtained when vagal resection has been combined with other operations such as gastro-enterostomy, or antrectomy, have prompted us to combine antrectomy with vagal resection in the next hundred cases, and in due time I trust we may have the opportunity to present the results of two parallel series; one showing the late results of vagal resection alone, and the other the results of the combined operation.

Dr. F. Avery Jones: Section of the vagus nerve is a logical sequence to the advances in our knowledge of the natural history of duodenal ulcer. It has been clearly recognized that disharmony with the environment plays an important rôle in the development, persistence or recurrence of duodenal ulcer.

Nervous tension is undoubtedly transmitted to the stomach via the vagus nerve and will stimulate particularly the inter-digestive secretion of acid and cause increased motility of the stomach. After cutting the nerve there is diminution of motility and of secretion, particularly between meals, and the volume and acidity of the nocturnal gastric secretion is reduced. The stomach will still respond to food and histamine stimulation, i.e. to hormonal and chemical stimulation, and the patients therefore still need proper diet. There is no longer an acid secretory response to hypoglycæmia from insulin and this enables us to test for completeness of the nerve section.

The development of a new surgical treatment at once raises the question of the scope for surgery in the management of duodenal ulcer. To what extent is medical treatment unsuccessful? My colleague, Dr. R. Doll, has been engaged in a field survey of peptic ulcer in different occupations and in interviewing 4,871 men in industry and transport or agriculture. The survey mainly covered London but was also conducted in a rural district and a small town. He found 148 who had, or had had, duodenal ulcer and they have been classified according to the present state of their dyspepsia and according to the type of treatment they had received. Some, indeed, had had no treatment and they were not diagnosed until X-rayed as a result of the survey.

	Total	Present ulcer symptoms			Number finally receiving surgical treatment
		None	Relapsing	Refractory	
<i>Medical treatment:</i>					
None	24	2	22	—	—
Home	58	15	36	7	(1)
Hospital	57	14	23	20	(12)
<i>Initial surgical treatment</i>	9	5	1	3	(2)

The intermediate group with amelioration of symptoms were men with recurring attacks of dyspepsia, often at fairly long intervals, and who were not losing much time from work. Many undoubtedly had recurrent ulceration. The refractory groups were men losing more than a month a year from work and subject to prolonged and severe bouts of dyspepsia.

Of those receiving medical treatment at home or in hospital, approximately 25% were entirely free from symptoms, 50% were having recurring attacks of mild or moderate severity and 25% were by all standards failures of whom half had a subsequent surgical operation with resulting cure in all but two cases.

The incidence of complications is another indication of the present inadequacy of medical control. In the survey, no less than 10% of the duodenal ulcers had perforated and 20% of them had bled, and this is the recognized incidence. Many of these complications had occurred while the patient was under medical supervision and even sometimes while in hospital. Illingworth *et al.* (1946) noted that 20% of their cases had re-perforated or bled within five years of the first perforation. It does seem that even with the best medical attention failure is to be expected in over a quarter of cases and there is therefore considerable scope for surgery. Even under ideal conditions at New Lodge and under the supervision of the late Sir Arthur Hurst, the final results were unsatisfactory and Barford (1928) reported 25% failures and 36% cures in a one to four years' follow-up of 90 cases.

Although the final results of medical treatment are unsatisfactory, nevertheless the initial response is excellent and in spite of a long history of dyspepsia, patients may obtain long-continued relief after a spell of medical care. Every case of uncomplicated duodenal ulcer is initially a medical problem and surgery is indicated only when the ulcer has become refractory or causes acute perforation or pyloric stenosis.

The rôle of a new surgical procedure must be considered in relation to the mortality of ulcer. Death occurs mainly from hæmorrhage or perforation and I have put together the deaths from these two causes at my hospital, 1945-6-7.

Age	No. admitted with hæmatemesis or perforation, 1945-6-7	Deaths	Percentage
20-29	22	—	—
30-39	41	3	4
40-49	72	2	
50-59	55	5	9
60-69	33	3	
70-79	25	8	32
80-	9	6	67

With modern treatment the mortality of major complications is low under 50 years of age and the need for elective surgery is much more to save the man's job than to save his life. Over 60, the need is certainly to save life in the face of possible complications. Although it is possible to achieve a mortality of 2 to 3% for partial gastrectomy, there are comparatively few surgeons in this class and 5% at least must represent the figures of the majority of surgeons. This is a high price for job-saving operations. As the operation is a major strain on the patient, there are many older patients who are not thought fit for it. Nevertheless, partial gastrectomy is a tremendous help in many cases but there is a great need for an operation with a low mortality and which imposes less strain on the elderly. Vagus nerve resection has a mortality of under 1% and in this respect meets our requirements.

Does vagotomy influence the disease process and improve the patient's prospect of full work? The results with duodenal and jejunal ulcer so far seem highly promising. My series, with my surgical colleagues, Mr. Ilyd James and Mr. J. D. Fergusson, is at present small. 48 cases have been done without a death but a number are too recent for any real assessment. Of these, 33 were done last year and 3 were for post-operative dyspepsias. They have since been reviewed. 30 were performed for duodenal ulcer. In the duodenal ulcer group, 2 cases have been unsuccessful; one has had a subsequent gastro-enterostomy for stenosis and the other has had continued pain but the insulin test showed an incomplete section of the nerve. 21 patients are perfectly well, their weight has increased, they are free from pain and have had no symptoms at all. The remaining 7 cases of duodenal ulcer have had varying degrees of discomfort, diarrhoea (7), which has persisted in 3 cases, occasional attacks which sound like hypoglycæmia (3), heartburn (1) and slight transient dysphagia (1). In spite of these symptoms, these patients, all with a long history of ulcer, profess themselves satisfied with the operation. The 3 cases with previous partial gastrectomy (2) or gastro-enterostomy (1) have not been satisfactory but all have a considerable functional overlay.

The unsatisfactory side-effects of the operation are undue gastric stasis, causing the halitosis and sense of fullness, diarrhoea, which usually clears up in a short time but may be quite severe and may occasionally persist, slight dysphagia with failure of relaxation of the lower end of the œsophagus and attacks which resemble hypoglycæmia. There may be persistence of ulcer pain if the nerve section is incomplete and pyloric stenosis may develop with the scarring of the healing ulcer. Finally, there may be persistence of symptoms from an associated psychoneurotic state. It seems probable that satisfactory results are obtained in 85-90% of cases, a proportion similar to the results after partial gastrectomy but achieved with a lower mortality.

Although the initial results are impressive these untoward effects are particularly disturbing because the intimate mechanism of the diarrhoea and of the "hypoglycæmic attacks" is at present unknown. It must be remembered that the intestine and pancreas are denervated by the operation. The question of gastric stasis is a further problem which needs study. It is possible that freer use of gastro-enterostomy will be needed, particularly when there is any indication of narrowing at the time of operation. Some are also advocating a limited gastrectomy plus vagotomy.

The position in this country to-day is that a number of surgeons have now had a limited experience of the operation. What we need is a really careful, well organized, well coordinated study in a number of centres. We need a central committee which can draw up a simple plan for routine recording of cases and of the follow-up. This needs to be done with the assistance of a statistician well versed in the modern methods of mechanical tabulation of results. With the taking over of hospitals, almoners should be able to undertake more follow-up studies and really careful proleptic series are urgently needed.

The careful planning and length of history and enable comparisons to be made between them down into age-groups and length of history and enable comparisons to be made between those with and those without gastro-enterostomy or antrectomy. The details of insulin tests and night-secretion tests could be standardized and would be a great help to busy

surgeons in other centres. Let us see that the appalling conflict of opinion over the results of gastric surgery in the past is not repeated over vagotomy. By good planning and team work, the treatment of bacterial endocarditis with penicillin was quickly worked out. It is just such a study that is urgently needed for vagotomy. Peptic ulcer is an important disease of modern life. Over 6% of men in industrial life have, or have had, ulceration and many continue to have recurring attacks. About 10% of the adult general medical or surgical beds in this country are occupied by patients with peptic ulcer.

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Mr. Rodney Maingot: After much investigation into the subject of vagotomy, I decided to apply the method to certain types of peptic ulcer which were recalcitrant to medical therapy and which, in my experience, yielded poor results with gastrojejunostomy or gastrectomy.

In spite of the flattering reception accorded by surgeons throughout the world to this newly resurrected operation, and the pleasing facility with which it can be accomplished with negligible mortality, it is my opinion that this procedure is being carried out at the present time too frequently and too light-heartedly.

If the experiment is worth while—and I am convinced that it is—then it should be undertaken only by those experienced in gastric surgery and who in addition hold responsible posts where every facility exists for research work.

Gastric ulcer.—Vagotomy should not be performed for chronic gastric ulcer. It is generally agreed that the correct treatment for a patient with a callous gastric ulcer is partial or subtotal gastrectomy; as the operative mortality is low, 3% or under, the subsequent onset of gastrojejunal ulceration is an extremely rare event, and the immediate and late results are excellent in every respect.

From every point of view the results of gastrectomy for gastric ulcer are superior to those which follow gastroduodenal resection for duodenal ulcer.

If a patient with a gastric ulcer cannot withstand resection, it is on the whole better to resort to medical therapy than to perform local excision of the ulcer alone or V-excision combined with gastrojejunostomy. Such operations not infrequently yield results as poor as those of medical treatment.

Although gastric ulcer is essentially a surgical condition, *medical in-patient treatment* for a period of one month is warranted if: (1) the patient is young; (2) there is a short history of indigestion; and (3) the ulcer is in the vertical part of the lesser curvature and is small. Healing should be demonstrated in one month and be confirmed at subsequent intervals varying according to the progress of the case.

A patient with a gastric ulcer has a cancer in his stomach until it has been proved otherwise. The ulcer is innocent if it heals staunchly as shown by gastroscopy and by radiology, and displays no signs of recurrence.

The recommendation has been made that vagotomy should be used as a therapeutic test for gastric ulcer—more especially the high cardinal ulcers, and for combined ulcers, the idea being that if the ulcer heals after vagotomy the lesion must be benign.

Then if it fails to heal, it is malignant and should be resected. "One may also agree that the patient is hardly to be blamed if after one major operation to deal with a gastric ulcer he refuses further surgery when told that his lack of response indicates that his stomach should have been taken out in the first place" (F. D. Moore, 1947, *Surg. Clin. N. Amer.*, 1078).

The most cogent reason for *not* employing vagotomy for cases of gastric ulcer is the fact that gastric ulcer is a recognized complication of this operation, especially when it is carried out as a primary procedure for uncomplicated duodenal ulcer.

To date I have had to perform subtotal gastrectomy on two occasions for simple penetrating gastric lesions which followed speedily in the wake of vagotomy for duodenal ulcer.

Duodenal ulcer.—My experience of vagotomy in this disease is limited to 46 cases during the last twenty-two months. All except two of the operations were for duodenal ulcer. There were: 23 simple vagotomies; 10 gastrojejunostomies combined with vagotomy; 11 gastrectomies combined with vagotomy; and 2 vagotomies for stomal ulcer following gastroduodenal resection for duodenal ulcer. There was one death in this small series.

Ogilvie once said that every operation upon the stomach is a success until it is found out.

At the Mayo Clinic in 1934 fully one-third of all cases of duodenal ulcer submitted to operation were pyloroplasties.

Now, fourteen years later, less than 1% of these cases are subjected to Judd's operation.

The rôle of a new surgical procedure must be considered in relation to the mortality of ulcer. Death occurs mainly from hæmorrhage or perforation and I have put together the deaths from these two causes at my hospital, 1945-6-7.

Age	No. admitted with hæmatemesis or perforation, 1945-6-7	Deaths	Percentage
20-29	22	—	—
30-39	41	3	4
40-49	72	2	
50-59	55	5	
60-69	33	3	9
70-79	25	8	
80-	9	6	32
			67

With modern treatment the mortality of major complications is low under 50 years of age and the need for elective surgery is much more to save the man's job than to save his life. Over 60, the need is certainly to save life in the face of possible complications. Although it is possible to achieve a mortality of 2 to 3% for partial gastrectomy, there are comparatively few surgeons in this class and 5% at least must represent the figures of the majority of surgeons. This is a high price for job-saving operations. As the operation is a major strain on the patient, there are many older patients who are not thought fit for it. Nevertheless, partial gastrectomy is a tremendous help in many cases but there is a great need for an operation with a low mortality and which imposes less strain on the elderly. Vagus nerve resection has a mortality of under 1% and in this respect meets our requirements.

Does vagotomy influence the disease process and improve the patient's prospect of full work? The results with duodenal and jejunal ulcer so far seem highly promising. My series, with my surgical colleagues, Mr. Iltyd James and Mr. J. D. Fergusson, is at present small. 48 cases have been done without a death but a number are too recent for any real assessment. Of these, 33 were done last year and 3 were for post-operative dyspepsias. They have since been reviewed. 30 were performed for duodenal ulcer. In the duodenal ulcer group, 2 cases have been unsuccessful; one has had a subsequent gastro-enterostomy for stenosis and the other has had continued pain but the insulin test showed an incomplete section of the nerve. 21 patients are perfectly well, their weight has increased, they are free from pain and have had no symptoms at all. The remaining 7 cases of duodenal ulcer have had varying degrees of discomfort, diarrhoea (7), which has persisted in 3 cases, occasional attacks which sound like hypoglycæmia (3), heartburn (1) and slight transient dysphagia (1). In spite of these symptoms, these patients, all with a long history of ulcer, profess themselves satisfied with the operation. The 3 cases with previous partial gastrectomy (2) or gastro-enterostomy (1) have not been satisfactory but all have a considerable functional overlay.

The unsatisfactory side-effects of the operation are undue gastric stasis, causing the halitosis and sense of fullness, diarrhoea, which usually clears up in a short time but may be quite severe and may occasionally persist, slight dysphagia with failure of relaxation of the lower end of the œsophagus and attacks which resemble hypoglycæmia. There may be persistence of ulcer pain if the nerve section is incomplete and pyloric stenosis may develop with the scarring of the healing ulcer. Finally, there may be persistence of symptoms from an associated psychoneurotic state. It seems probable that satisfactory results are obtained in 85-90% of cases, a proportion similar to the results after partial gastrectomy but achieved with a lower mortality.

Although the initial results are impressive these untoward effects are particularly disturbing because the intimate mechanism of the diarrhoea and of the 'hypoglycæmic attacks' is at present unknown. It must be remembered that the intestine and pancreas are denervated by the operation. The question of gastric stasis is a further problem which needs study. It is possible that freer use of gastro-enterostomy will be needed, particularly when there is any indication of narrowing at the time of operation. Some are also advocating a limited gastrectomy plus vagotomy.

The position in this country to-day is that a number of surgeons have now had a limited experience of the operation. What we need is a really careful, well organized, well co-ordinated study in a number of centres. We need a central committee which can draw up a simple plan for routine recording of cases and of the follow-up. This needs to be done with the assistance of a statistician well versed in the modern methods of mechanical tabulation of results. With the taking over of hospitals, almoners should be able to undertake more follow-up studies and really careful proleptic series are urgently needed.

The careful planning and central collection of 500-1,000 cases would enable us to break them down into age-groups and length of history and enable comparisons to be made between those with and those without gastro-enterostomy or antrectomy. The details of insulin tests and night-secretion tests could be standardized and would be a great help to busy

There were 37 such cases reported by Waltman Walters (personal communication, January 1948) with good results in 31, fair results in 5, and poor results in 1.

I do not advise transthoracic vagotomy for the last-mentioned type of case, as I believe that by the abdominal route large segments of the right and left vagus nerves can be resected after the surgeon has assured himself that the amount of stomach removed is adequate, that no pyloric stump with its baneful mucous lining is left behind, and that the stoma is adequate and well placed, that there is no obstruction of the proximal or distal jejunal limbs, and that a gastro-jejuno-colic fistula can be excluded with safety.

I would not recommend vagotomy for anastomotic ulcer following gastrojejunostomy, because the mechanics of this procedure are so often at fault, and even if healing of the lesion does eventuate this is often followed by excessive and progressive scar formation at the site of the all-too-frequently contracted stoma. The healing of the ulcer, the tardy emptying of the stomach, and the added pyloric spasm may precipitate a condition of malnutrition complicated by a low-grade small-gut obstruction.

Technique of vagotomy.—The operation may be performed through the chest or through the abdomen. If the operator is a thoracic surgeon or one interested in thoracic surgery, he will perform the operation through the chest; if, on the other hand, he has specialized in abdominal surgery, and more particularly if he is a general surgeon, he will select the epigastric route.

I would criticize the transthoracic approach on these grounds: (1) The lesion cannot be examined (possibly malignant). (2) Pyloric obstruction cannot be corrected. (3) Post-operative pain in the incision and costo-vertebral joint may result. (4) Gastrojejunostomy is a difficult and unsatisfactory procedure when performed as a secondary operation on a dilated, oedematous and atonic stomach. (5) Intrathoracic complications (empyema) may result.

Mr. David H. Patey: Though Dragstedt in 1943 with his paper on vagotomy in the treatment of peptic ulcer reopened the whole question of the surgical treatment of peptic ulcer, it is still too soon for any final conclusions on the position of vagotomy in the treatment of peptic ulcer. My own experience is of 31 cases the first of which was operated on in November 1945. I have regarded them as research cases, and have carried out full pre- and post-operative tests. As a result of my experiences I should like to make a few brief observations under three headings: Surgical anatomy, complications, and results.

Surgical anatomy.—The abdominal route is, with the possible exception of certain cases of gastrojejunal ulcer, better than the thoracic for the main reason that it enables the condition of the ulcer to be examined, and if necessary additional operative procedures to be performed to deal with the mechanical sequelæ of peptic ulceration. A minor additional reason in favour of the abdominal route is that sometimes following the thoracic approach the patient has temporary neuritic pains in the epigastrium from trauma to intercostal nerves which is of little significance in itself but which he may interpret as a persistence of his visceral troubles. When I have used the thoracic route, I have preferred a right-sided approach to a left-sided. I have found touch as well as sight valuable for identification of the vagus with the intra-abdominal approach, since this nerve may lie in the cellular tissue quite a distance from the œsophagus. The nerves offer a resistance to touch quite different from that of the cellular tissue.

Complications, or perhaps, more accurately, sequelæ: I have had cases with temporary trouble from diarrhœa, duodenal ileus, cardiospasm, attacks of giddiness due to transient hypoglycæmia, and foul eructations. These sequelæ are usually only temporary, cause only a minor degree of disability, can in part be alleviated by correct post-operative treatment, and in no way should condemn the operation or lead to its abandonment if the results on the ulcer itself should prove satisfactory.

Results.—In 5 cases where the operation was performed for gastrojejunal ulcer, the results have so far been good. 2 cases bear on the problem of gastric ulcer: one was that of a combined gastric and duodenal ulcer. Following vagotomy the duodenal ulcer healed but the gastric ulcer got progressively larger and was eventually excised by a partial gastrectomy. The other case was that of a vagotomy for duodenal ulcer in which a gastric ulcer developed subsequent to the operation. From these two experiences, and in view of the general good results of gastrectomy in gastric ulcer, I decided not to do any more vagotomies for gastric ulcer. Of the remaining 24 cases, which were of duodenal ulcer, 4 cases were failures in that symptoms persisted and X-rays still showed active duodenal ulcers. In 2 of these cases there was evidence that vagotomy was not in fact achieved, so that they must be

It has taken nearly fifty years to appreciate the fact that in duodenal ulcer *gastrojejunostomy* is a damning procedure when carried out in young patients, in those with uncomplicated lesions associated with marked hyperchlorhydria, in those with recurrent hæmorrhages, in psychoneurotics, and in patients with intractable ulcers.

Gastrojejunostomy should be reserved for aged and feeble patients with obstructive symptoms or severe pain due to a deeply penetrating duodenal ulcer, and for those who are in a poor general state of health due to some concomitant lesion which would render gastric resection too hazardous (R. S. Boles, 1948, *J. Amer. med. Ass.*, 136, 764).

I do not therefore advise vagotomy combined with gastrojejunostomy for the unresponsive duodenal ulcer, as the post-operative convalescence in my series of cases has been prolonged and stormy, and it takes weeks or long months for the flabby, distended, atonic stomach to empty its decomposing contents into the patulous unreceptive jejunal stoma.

Diarrhœa, ileus, colic, dysphagia, and the belching of malodorous gases have been troublesome sequelæ in the majority of cases. I agree with Lewishon that pronounced atony is one of the most dangerous complications following abdominal operations. Four of my patients developed well-marked cardiospasm within one week following vagotomy for duodenal ulcer, which, however, responded to dilatation with œsophageal bougies or treatment with octyl nitrite.

I do not believe that the new physiologic operation of pyloro-duodenectomy or antrectomy followed by the Polya type of anastomosis combined with vagotomy will improve the late results, since we are as yet ignorant of the exact anatomical distribution of the "humoral" elements in the stomach, and gastric neurectomy leaves the large residual gastric pouch sullen and toneless.

Subtotal gastrectomy—the removal of at least five-sixths of the stomach together with the ulcer in the duodenum, adopting the antecolic Polya-Hoffmeister procedure, is a seasoned, highly perfected and gratifying procedure when performed for duodenal ulcer, yielding a high percentage of lasting cures.

The higher the resection, the fewer are the number of subsequent secondary ulcers. In expert hands the incidence of gastrojejunal ulcer is about 3%. This figure may be lowered by a complementary vagotomy, and more especially in that treacherous type of case associated with recurrent hæmorrhages and markedly raised acid values in the gastric juice.

The higher the resection, the greater is the loss of weight. Following subtotal gastrectomy patients are slow to gain in weight.

Insulin test.—All authorities are agreed that Hollander's insulin test is a reliable one in ascertaining post-operatively whether all the vagal branches to the stomach have been well and truly resected.

The test in its present form is not free from the danger of insulin shock and other alarming phenomena. There were cases in which I was certain I had sectioned all the nerves, and yet the test was positive; in others again I performed what I considered to be an unsatisfactory and incomplete gastric neurectomy, and to my surprise the test was negative.

I have had patients who after simple vagotomy for duodenal ulcer gave a negative response shortly after operation and in whom six months later the test was positive. Although the insulin test revealed that in the majority of my patients the nerves had been completely sectioned, nevertheless there did not appear to be any relationship between the completeness and incompleteness of the vagotomy and the relief of pain, the acidity figures, the motor disturbances and the other complications.

Indications for vagotomy.—Because the results are so unpredictable and variable, I would now advise vagotomy for the following types of cases: (1) Nervous patients under the age of 45 with uncomplicated duodenal ulcer (no history of recurrent hæmorrhages and no evidence of obstruction), in whom repeated courses of treatment in hospital have failed to effect a cure. Here the lesion is often puny and out of all proportion to the symptoms and may rightly be deemed to be unworthy of a pyloroplasty or a grandiose gastroduodenal resection.

(2) Cases of chronic duodenal ulcer which give a history of repeated bleedings. Here vagotomy is combined with subtotal gastrectomy to safeguard the patient against the real danger of stomal ulceration or recurrent hæmorrhages.

(3) Cases of gastrojejunal ulcer which have followed a well-performed gastroduodenal resection. This is the prime indication for vagotomy.

The immediate and interim results following vagotomy for an anastomotic ulcer after gastroduodenal resection are excellent in every respect. Pain is instantly relieved, the ulcer heals with dramatic rapidity, and the longing for food is restored.

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regarded as technical failures. In the other 2 cases, however, the ulcers persisted in spite of technically successful vagotomies.

At subsequent operations for excision of the ulcers, in one case an adherent callous ulcer 2 cm. in diameter was found and in the other a similar ulcer 1.3 cm. in diameter. From this experience I concluded that vagotomy alone was not sufficient in large callous ulcers. In the remaining 20 cases of duodenal ulcer, the results up to the present are satisfactory although it should be emphasized once again that in no case has the follow-up been very long and that some of the cases are very recent. These 20 cases fall into two approximately equal groups. In the first, the ulcers were small—either no induration was present or the induration was less than 1 cm. in diameter—and there was no cicatricial narrowing of the duodenal lumen. In this group vagotomy only was performed. In the second, there was either a large callous ulcer of the duodenum or cicatricial narrowing of the lumen. In this group in addition to the vagotomy a duodeno-pylorotomy with end-to-end anastomosis has been the standard operation performed. The amount of tissue excised has been small, on the stomach side the section running immediately proximal to the pyloric sphincter and on the duodenal side the section being made immediately beyond the ulcer after the duodenum had been sufficiently freed to enable a direct end-to-end anastomosis to be made after resection. The tissue excised has been about 21 to 42 grammes, so that any good results that may be obtained cannot be attributed to a gastrectomy effect. While local conditions may exceptionally indicate gastro-enterostomy rather than pyloro-duodenectomy, I feel that wholesale gastro-enterostomies would be unwise, particularly as my experience has been (and I know it is the exact reverse of what is generally taught) that, in cases of pyloric stenosis especially, gastro-enterostomy is liable to be followed by anastomotic ulceration. The counter-argument might rightly be made of the generally good results so far from vagotomy in gastrojejunal ulcers but I think it would be wrong to revive as a standard procedure an operation like gastro-enterostomy, the complications of which have proved such a trial to surgery for so many years, without strong proof of the long-term value of vagotomy.

My tentative conclusions are that vagotomy has no place in the treatment of gastric ulcer; it may have an important place in gastrojejunal ulcer, and its possible place in duodenal ulcer is worthy of further exploration. But alone it is not sufficient to cure large callous duodenal ulcers and it is clearly inadequate alone in the presence of mechanical complications such as stenosis.

Mr. Bryan N. Brooke: In the first 50 cases of a series of vagal sections performed by the Surgical Unit at the Queen Elizabeth Hospital, Birmingham, there were 51 lesions including 43 duodenal, 5 gastric, 2 anastomotic ulcers, and 1 gastro-jejuno-colic fistula. The operations performed were:

Thoracic	Abdominal
28	9
	+ Gastro-enterostomy
	11
	+ Pyloroplasty
	2

The "drainage" operations were all premeditated and performed at the time of the nerve section; gastro-enterostomy has never had to be performed as an emergency to relieve retention.

The gruel test meal, night resting juice and insulin test are performed, repeated immediately post-operatively, and again at a six-month follow-up when the patient is readmitted for three nights. The insulin test is not regarded as entirely satisfactory, for there is no certain indication that the full vagal reflex has been brought into play in the post-operative case with a negative response, unless the hypoglycæmia symptom of sweating can be accepted as a signal of this. Hollander's figure of a blood-sugar level of 50 mg. is arbitrary and unacceptable, particularly when judged against sweating (figures were presented to illustrate this argument). The dose of 0.1 unit per kilo body-weight has been found satisfactory, when judged either by sweating or by Hollander's standard, except immediately post-operatively when more insulin appears to be required to lower the blood sugar to the same extent (examples were given).

The usual arguments regarding approach prevail with us, the balance having to be struck between the advantage of the less uncertain section by the thoracic approach, and the diagnostic advantages of the abdominal approach together with assessment of stenosis which the laparotomy permits. Pleural adhesions do not cause insuperable difficulty, but hiatus hernia, encountered three times and not displayed by previous X-ray, is disconcerting from the abdominal approach.

No deaths have occurred. Chest complications were as follows:

Approach	Cases	Pul. collapse	Effusion
Thoracic ..	28	12	16 (4 required aspiration. No empyema)
Abdominal	22	7	0

There were no cases of persistent gastric retention and only 2 patients vomited in the immediate post-operative period. Persistent diarrhoea occurred in 5 cases. This is in clear contrast to the American reports, for in their series gastric retention and diarrhoea are notably higher. Perhaps this is the result of the higher fat content of their diet, for a recent report shows that the diarrhoea may be a steatorrhoea; the fat may further slow down the emptying of an atonic stomach. Nine patients experienced a sense of obstruction to swallowing, one returning to hospital two weeks after discharge with this complaint. Barium swallow showed no achalasia, nor any "hold-up". This symptom corrects itself without treatment. Likewise foul eructation has corrected itself in three to six months in the eight patients who have complained of it.

One possible autonomic complication has been encountered. In view of the imbalance in favour of the sympathetic system brought about by cutting the vagus, the blood-pressure has been recorded at follow-up in all cases. One patient of 50 had a blood-pressure of 130/90, before operation; three months later it was 198/120, and after six months, when the patient was admitted for three days, it was persistently 210/130. This patient had no headaches and no albuminuria.¹

With 35 cases followed up and only 18 seen at six months, too little evidence has yet been collected to judge the effects of section on peptic ulcer.

Mr. H. Daintree Johnson (*Précis*): Of the 115 patients operated on by Mr. Orr and myself I have submitted 52 to intensive investigation and personal follow-up.

Investigation of spontaneous night secretion, as well as insulin test, is carried out before and after operation in all cases. Some have half-hourly gastric aspirations for twenty-four hours while on a normal diet and the H ion concentration of the samples is measured electrically. This investigation has confirmed that it is during the night, when the buffering action of food is absent, that gastric acidity reaches its highest levels.

After vagotomy there is a reduction by 77% of the average free acidity in the night secretion. Volumes are probably at least as important as acid levels and these are reduced on the average by 74%.

The reduction in H ion concentration averages 99.8%, represented by a rise in pH from 2 to 4.7. The amount of free HCl in grammes in the whole of the night secretion is probably the most valuable figure and this is reduced by 96% on the average (Table I).

TABLE I.—SPONTANEOUS NIGHT SECRETION IN 40 CASES OF DUODENAL ULCER, BEFORE AND TWO TO THREE WEEKS AFTER VAGOTOMY

	Before operation	After vagotomy
Average free HCl, ml. N/10 ..	53	12
range	10-91	0-32
Average peak free HCl	80	31
range	26-116	0-74
Average total volume, mls. ..	522	137
range	187-1,115	23-290
Average pH	2.0	4.7
range	1.1-3.2	1.9-8.0
Average free HCl in grammes in whole night secretion ..	1.01	0.05
range	0.11-2.47	0.0-0.14

Out of 95 patients with peptic ulcer submitted to insulin test before operation 9 failed to respond, though 5 reacted normally when tested again with the same dose of insulin. A single negative insulin test is therefore not a proof of complete vagotomy. Some have

¹Bilateral hydronephrosis has since been demonstrated in this case. The time of onset of the hypertension may be coincidental, or the hypertension may have been precipitated by vagal section in a patient previously disposed towards it.

attempted to employ the insulin test before operation as an index of "vagotonia". It is true that the gastric insulin response is typically high in duodenal ulcer patients, but if indeed neurogenic secretion is an important factor in the aetiology of duodenal ulcer, as I believe it to be, then I would suggest that it is the amount of vagal activity that is likely to be at fault, rather than the secretory response to a single and, in a sense, unphysiological stimulation of the vagus. The estimation of the spontaneous night secretion of acid is probably a better index of spontaneous vagal activity.

To employ the histamine test, as some have done, to assess the effects of vagotomy would seem quite irrational. It is one of the virtues of vagotomy that, unlike gastrectomy, it reduces the dangerous resting secretion without having any direct effect on hormonal secretion produced in response to the taking of food and essential to its proper digestion.

Motor effects.—It has been shown by many workers from Pavlov to Teorrel that acid which remains in the stomach is slowly eliminated, probably by a variety of mechanisms. The rapidly emptying stomach in duodenal ulcer hurries acid on into the duodenum before these mechanisms have had time to operate. For this reason the delay in gastric emptying which results from vagotomy is probably one of its most important curative effects. Also the protective buffering action of food is prolonged.

Diarrhœa.—The incidence of diarrhœa can be correlated with the degree of hypochlorhydria. It has not occurred in any patient whose insulin test was still positive or equivocal after operation, but transitory diarrhœa has occurred in one in three of those whose vagotomy appeared to be complete. Large doses of hydrochloric acid have failed to relieve the condition, but in two cases precipitated ulcer pain. Sulphasuxidine is more successful but not consistently so. There is no relation between the incidence of diarrhœa and the rate of gastric emptying.

Dysphagia.—"Slow swallowing" is a common complaint for a short time after operation and may be traumatic. One patient had dysphagia which took three months to clear up. X-ray showed the appearance of achalasia of the cardia and relief was obtained from octyl nitrite inhalation.

Persistent deformity of the duodenal bulb.—Deformity may be due to either spasm or scarring. The former disappears after vagotomy. The latter is part of the healing process and may increase. 8 patients showing increasing X-ray deformity are all symptom free. 2 of these still have the appearance of a crater.

Hypoglycæmia.—About one-third of the patients have attacks of weakness, sweating and faintness which often pass off in a few weeks. Two patients investigated had hypoglycæmia during an attack.

Body-weight.—Weight gain was considerably superior to that of a group of gastrectomized patients followed during the same period (Table II).

TABLE II.—BODY-WEIGHT

	18 vagotomy patients st. lb.	21 gastrectomy patients st. lb.
Average "normal" weight	10 1	10 2
Average pre-operative weight	9 0	9 0
Average weight six months after operation ..	9 11	8 12
Average weight one year after operation ..	9 13	8 13

Almost without exception the complications of vagotomy in our series have been transitory. I am still of the opinion that pure vagotomy is a more justifiable operation for uncomplicated but recalcitrant duodenal ulcer than pure gastrectomy.

To perform gastrectomy and reserve vagotomy for the anastomotic recurrences seems to me less rational than to try vagotomy first and keep gastrectomy for those in whom vagotomy fails to give permanent relief. In this way the more dangerous operation is used less often and the overall mortality should be reduced.

With deeply penetrating or stenosing ulcers my experience with combined vagotomy, antrectomy and removal of the ulcer is so far most encouraging.

Dr. J. Jacques Spira: Vagal resection for peptic ulcer.—Criticism of vagal resection for peptic ulcer cannot be attempted without reference to the physiological principles which regulate gastric function; the misinterpretation of the role played by hydrochloric acid in the pathogenesis of ulcer is, in my opinion, mainly responsible for the present confusion and the consequent failure to find a solution of the problem.

A review of the literature reveals that treatment is solely concerned with the elimination of the acid factor held to be responsible for the causation of the ulcer. In view of the important role which hydrochloric acid plays in the metabolism of the body, it is questionable whether the establishment of a permanent achlorhydria, which is difficult to achieve in practice, is at all desirable.

While ulcer does not occur in the absence of acid, chronic ulcer is invariably associated with an excess of gastric secretion. Hydrochloric acid, however, cannot by itself produce the ulcer, the gastric mucosa must first be damaged before the acid can have its destructive effect but the presence of acid does not delay healing (Bolton, 1913). Prolonged night secretion which has been blamed for ulcer causation can be controlled medically by the continuous drip method without alkalis (Winkelstein, 1932) but is tedious and does not prevent recurrence; according to Sandweiss (1946) and Voegtlin (1947) normal and ulcer patients have similar nocturnal secretions. Surgery now advocates a drastic "measured radical gastrectomy" which leaves only a small devascularized remnant (Visick, 1948).

Dragstedt and Owens (1943) introduced vagotomy because Hartzell's (1929) experiments suggested a neurogenic origin for the excessive gastric secretions, but Vanzant (1931) found that two years later the gastric secretions of Hartzell's dogs had returned to normal. In the human, gastric secretions return to normal six to twelve months after vagotomy (Moore *et al.*, 1947); if not, the patient requires parasympathomimetic drugs to counteract the gastric atony (Stein *et al.*, 1947).

It should be remembered that the secretory and motor functions of the stomach cannot be dissociated and that they respond simultaneously to stimulation or to inhibition.

Normally, mechanical trauma alone fails to produce ulcer. The maintenance of continuous hypermotility and hypersecretion does not produce chronic ulcer (Orndorff *et al.*, 1935) neither does anastomosis of the oesophagus to the duodenum after total gastrectomy (Ivy *et al.*, 1931) while a rough diet after bilateral vagotomy produces ulceration (Beazell and Ivy, 1936). Vagotomy shortens the survival period of Mann-Williamson dogs (Saltzstein, 1948) and does not prevent the occurrence of ulcer (Beaver and Mann, 1931) which it may produce experimentally (Greggio, 1916).

The role of hydrochloric acid as a basis for the classification of peptic ulcer.—The association of hydrochloric acid with gastroduodenal ulcer provides the basis of a classification of peptic ulcers:

(1) It distinguishes between the acute and chronic lesions: (i) Acute ulcer occurs in the presence of normal or diminished acid values: hydrochloric acid takes no part in its production; (ii) chronic ulcer is invariably associated with high acid values: hydrochloric acid is an essential element in its production.

These two varieties of ulcer are aetiologically unrelated to each other.

(2) It subdivides chronic ulcers into two categories according to whether they are situated in (i) an acid milieu, or (ii) an alkaline milieu.

These two varieties of ulcer are aetiologically unrelated to each other.

The former is strictly limited to the stomach and the first part of the duodenum while the latter affects the rest of the intestinal tract. Hydrochloric acid has no injurious effect on the normal mucous membrane of the "ulcer-bearing" area in the acid milieu and *a priori* cannot be the only factor concerned in ulcer formation. It is, however, strongly destructive of the mucous membrane of the alkaline milieu outside the "ulcer-bearing" area, its effect varying directly as the distance from the pylorus (McMaster, 1934); it is the only factor responsible for the production of the oesophageal ulcer, Meckel's diverticulum ulcer and the gastrojejunal ulcer. Ulceration does not take place in the aberrant gastric mucosa but in the tissue immediately adjacent to it.

With the exception of the gastrojejunal ulcer, true chronic ulcer as seen in man has not been reproduced experimentally (Ivy, 1946). Dragstedt (Dragstedt and Schafer, 1945) commits his initial error by assuming that the gastrojejunal ulcer artificially produced in the alkaline milieu is analogous to the ulcer which occurs spontaneously in the acid milieu and he applies his observations on experimental ulcer to all other types of peptic ulcer. He argues from the particular to the general and is led to postulate untenable premises from which he deduces inadmissible conclusions.

To summarize.—A procedure which is fraught with grave operative risks and is based on the erroneous interpretation of observed facts, which abolishes the nervous control of the gut and its sphincters and completely disorganizes its natural reactions and which, in addition, interferes with the normal responses of the gall-bladder, pancreas and kidneys, cannot claim the support of physiological principles in justification of a surgical experiment on the human.

The suggestion (Boles, 1948) that surgeons should declare a moratorium for vagotomy for five years should be imposed forthwith.

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Mr. Eric M. Nanson for Mr. Norman C. Tanner: In 24 cases of peptic ulcer, mainly duodenal in site, we have employed vagal resection; the follow-up period ranged from one month to fourteen months. The ages ranged from 19 years to 65 years, the larger number being in the 30–40 age-group. Males predominated over females by 19–5. The duration of symptoms previous to operation varied from one year to thirty years, the average duration being five to ten years. The mortality rate was nil.

Post-operative follow-up showed 10 cases satisfactory in all respects. The most serious and frequent complication was diarrhoea which persisted in one case up to six months, and, characteristically, occurred in the early mornings.

The selection of cases suitable for operation is essentially clinical—the insulin test meal is not a test used in selection. Insulin test meal was used in all cases post-operatively to test the completeness of the operation. We used 15 units of insulin intravenously in all cases and always got a satisfactory hypoglycæmia.

Other post-operative complications noted were tachycardia within twelve to twenty-four hours, and evidence of peripheral circulatory failure. Distension and ileus coming on after thirty-six hours was also noted in a few cases.

The operation of vagotomy for peptic ulcer is still an experimental procedure. If there is an obstructive element present, it would be more effective to do a pyloroplasty rather than a gastrojejunostomy in order to limit the introduction of complicating factors.

Clinical Section

President—G. E. VILVANDRÉ

[April 9, 1948]

MEETING HELD AT ST. JAMES' HOSPITAL, BALHAM, LONDON, S.W.12

Chronic Cyclical Granulopenia.—B. BARLING, M.D.

E. R., female aged 32. This case was reported to the Clinical Section in November 1943 (*Proc. R. Soc. Med.*, 1944, 37, 86).

Since the age of 12 she has complained of ulcers of the mouth recurring at irregular intervals of three to four weeks. The ulcers are shallow and painful. Situated on the tongue, under the tongue, on the mucous membrane of the cheek and also at the angles of the mouth. The average duration of the ulcers is about two weeks, but when they become deep and widespread they may take months to heal. Ulcers at the corners of the mouth involve all tissues and have the appearance of a bloodless excision of tissue about the size of a half-penny. The healing is slow with marked scarring.

In 1944 she became pregnant and during this period the ulceration of the mouth became more persistent and for the first and only time she had vulval ulcers.

The delivery was normal and the child is well. On and off since then she has had ulcers of the mouth and tongue of varying severity. Nine months ago she developed two large painful ulcers on the back of the right leg just above the heel. They have resisted all attempts at healing.

Past history.—Tonsillitis frequently until 1940, when tonsillectomy was performed; no infection since then. No other illnesses.

Family history.—No relevant facts.

Physical examination reveals no abnormalities except the scarring at the corners of the mouth and the apparently healing leg ulcers.

No splenic or hepatic enlargement, no palpable glands.

Blood examination has shown a variable but persistent low level of the cells of the granular series. No anaemia or abnormality of red cells. It has been noted, however, that when the total white cells fall, which is due to a reduction in the granulocytes, the ulcers appear.

The sternal marrow is normal.

Section of a fragment of one of the ulcers of the leg shows fibrous pyogenic granulomatous inflammation of the skin of leg. A blood-count was done after an injection of adrenaline with no change in the count. She is well except for the troublesome recurrent ulcers of the mouth and the ulcers of the leg which do not heal.

She has been treated with liver, hog's stomach, nicotinic acid, pyridoxin, pentnucleotide, nucleic acid, yellow bone-marrow extract and iron, but has failed to show any response.

Blood-counts were as follows:

		W.B.C.	Polymorphs. %	Eosinos. %	Lymphos. %	Monos. %
18.4.41	..	6,800	52	—	36	12
29.5.42	..	1,300	26.5	0.5	60	13.5
3.11.43	..	3,600	25	4	59	11.5
29.3.44	..	2,760	15	3	57	24
28.8.47	..	3,800	31	10	35	24
24.3.48	..	4,800	60	—	30	9

The advisability of splenectomy was discussed.

OCT.—CLIN. 1

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The test was carried out in order to ascertain whether the spleen was storing and then destroying the granulocytes, the so-called "cannibal spleen". Had this been established benefit might have accrued from splenectomy, which we have been reluctant to consider because of her excellent health and complete absence of symptoms.

Dr. F. Parkes Weber considered that in both cases splenectomy would be unwise and a "jump in the dark".

Acromegaly and Pluriglandular Dysfunction showing Calcification of Pituitary.—A. G. LEISHMAN, M.B. (for A. KAHAN, M.D.).

Mrs. S. P., aged 46.

History of present condition.—1931: Became anxious after death of child in accident. 1932: Onset of symptoms of thyrotoxicosis and tracheal pressure. 1939: Early acromegaly, recognizable in photograph. 1940: Removal of cystic adenoma of thyroid (? partial thyroidectomy) followed by rapid development of florid acromegaly. 1941: Diabetes mellitus discovered.

One week before admission she developed sudden loss of speech, asymmetry of face and became confused.

Family history.—Father subject to gout. Sister had fits in childhood. Married, with two sons.

On examination.—Typical acromegalic facies. Slight proptosis on left. Fundi: Veins full, no other abnormality. Left fundus partly obscured by immature cataract. Visual fields: Right normal. Left, gross temporal and upper nasal quadrantic defect.

Abdominal reflex absent, and plantar response extensor, on right side.

Urine: Severe glycosuria and ketonuria. (She had discontinued taking insulin one year previously, because of abscesses.)



FIG. 1.—Pituitary fossa showing enlargement and central calcification.

Z.P.I. 32, Soluble Insulin 44, o.m. (180 grammes carbohydrate).

Comment.—The association of acromegaly with outspoken evidence of pluriglandular dysfunction as shown by this case is well recognized. The correlation of an only moderately enlarged sella with Jacksonian seizures and evidence of intrasellar calcification is less easy. No record was found of even large acidophil adenomas causing fits nor of undergoing calcification. The family history suggests that this patient may have a congenital low cerebral "threshold" for epilepsy.

Calcification, and osseous metaplasia occur frequently in slowly growing squamous-cell carcinomata of the craniopharyngeal tract (squamous adamantinoma, &c.), but no record was found of such tumours producing an acromegalic syndrome. Whatever the pathology the presence of calcification in association with a clinical picture of continued anterior lobe hypersecretion is of interest.

POSTSCRIPT (September 1948).—This patient has now completed a course of deep X-irradiation of the pituitary fossa with striking symptomatic improvement and some increase of the visual fields.—A. G. L.

Investigations.—Blood-count normal. Blood urea 53 mg. %. Plasma cholesterol 218 mg. %. C.S.F. (two examinations): Protein 50 mg. %, pressure normal. W.R. negative in blood and C.S.F. X-ray: Sella moderately enlarged, posterior clinoid processes thinned and rarefied. Rounded opacity in sella approximately 1.0×0.8 cm. demonstrated stereoscopically (fig. 1). Pineal body in normal position. Moderate bony changes of face. Phalanges thickened and characteristically "tufted".

Progress.—She had frequent Jacksonian convulsions involving right side of face for periods of four days during two admissions and associated with aphasia, Todd's paralysis and transient hemiplegic signs. All resolved except minimal right facial weakness on discharge. Diabetes moderately well stabilized on

Dr. F. Parkes Weber referred to Dr. Dennis Embleton's case (which he remembered) of "Rhythmic Neutropenia with Recurrent Buccal Ulceration" (*Proc. Roy. Soc. Med.*, 1937, 30, 980). He also referred to "Behcet's Syndrome"—recurrent ulceration of the oral and genital mucosæ, sometimes associated with recurrent iritis and hypopyon (I. Katzenellenbogen, *Brit. J. Derm.*, 1946, 58, 161).

Chronic Granulopenia.—B. BARLING, M.D.

M. W., female aged 17. This girl was admitted to the Grove Hospital in June 1945 as a case of gastro-enteritis. She had marked pallor and a temperature range of 98–103° F.

Investigation.—Fæces: No pathogenic bacteria. Urine: Some epithelial cells, sterile, acid, trace of protein, no sugar. Blood: Culture gave no growth; agglutinations negative for enteric group, dysentery group, abortus, non-specific salmonella. Sputum: No tubercle bacilli seen.

Blood-count.—22.6.45: R.B.C. 1,460,000; Hb 32%; C.I. 1.1; W.B.C. 6,400 (polys. 5%, lymphos. 92%, monos. 3%). Platelets: normal number, cell diameter 7.5 μ . Some anisocytosis and slight poikilocytosis.

Sternal puncture showed normal cell content.

29.6.45: She was transferred to St. James' Hospital. Apart from the history above, the mother stated that the girl had not been well for a year and that during that time she had complained of tiredness, lack of energy and more recently her mother had noticed pallor, anorexia and shortness of breath.

The mother also stated that the child had had tonsillectomy performed four times.

On examination.—She was pale with a temperature of 102.4° and pulse-rate of 124. The liver was just palpable and the spleen was easily palpable. There were no enlarged glands, no purpura. Fundi were normal. No other physical signs.

The blood-count was as follows.—R.B.C. 1,540,000; Hb 25%; C.I. 0.8; W.B.C. 3,200 (polys. 10%, lymphos. 89%, monos. 1%). Anisocytosis, poikilocytosis, slight polychromasia, platelets 231,100 per c.mm. Red cells: fragility normal.

She was given a blood transfusion of 3 pints which brought her blood up to: R.B.C. 2,690,000; Hb 58%; C.I. 1.1, W.B.C. 3,200 (polys. 11%, lymphos. 88%, monos. 1%). Bleeding time and coagulation time normal.

The blood culture was sterile. Van den Bergh 0.4 unit; Kahn negative. The temperature continued to be raised and her blood had to be kept up by transfusions from which at times she had reactions.

E.N.T. report: Some post-tonsillectomy scarrings and pharyngitis sicca. Nose and ears: N.A.D.

She was treated in addition to the transfusions with iron, intramuscular injections of liver and pentnucleotide 10 c.c. b.d. but with no obvious improvement.

4.8.45: She developed pneumonia consolidation at the right base, but her white cells remained at 4,500 and polys. 12%.

She was treated with penicillin but the condition showed no change and she appeared to be rapidly losing ground. However, as she is an only child, on 10.8.45 her mother decided to take her home which she did by ambulance.

Three weeks later she was readmitted for a blood transfusion—on admission the count was: R.B.C. 1,580,000; Hb 37%; C.I. 1.15; W.B.C. 4,600 (polys. 16%).

Since then she has been on large doses of proteolysed liver and iron and her hæmoglobin and red cells have been kept at approximately normal levels. Although the total white cells have occasionally exceeded 10,000 the percentage of granulocytes has rarely reached 10% of the total.

Throughout the past two and a half years she has kept in good health and developed normally. There are no physical signs except for a steady increase in the size of the spleen. She was given an injection of adrenaline and white cell counts were taken before and after. There was a rise in the total leucocytes, but the percentage of granulocytes did not increase.

Mr. A. M. Desmond: It is important to determine what relationship multiple carcinomata, presenting as in this case, bear to polyposis of the colon. It is advised that in polyposis, as malignancy usually occurs in the distal bowel, this event should be awaited and an abdomino-perineal resection then performed. The distal bowel is then observed by sigmoidoscopy through the terminal inguinal colostomy, subsequent resections being carried out if indicated. In this case, the first malignant growth occurred in the caecum and later two others in the pelvic colon; in other words a reversal of the sequence of events stated to occur in polyposis. I therefore feel that as in 25% or more of patients suffering from polyposis, malignant change takes place, more radical measures should be adopted.

Mr. Norman C. Tanner: In this case we performed a Mikulicz type of colonic resection, though our usual procedure is to make a defunctioning proximal colostomy, followed by a radical resection of the colon and end-to-end anastomosis. This has proved to be very suitable, even for aged people, for two nonagenarians and several octogenarians have survived it without difficulty. At one time I used aseptic anastomoses, but stenosis of the anastomosis complicated one or two cases and so I changed to open end-to-end suture with good mucosal apposition. We have never had a general or local peritonitis following this procedure and I do not believe that the slight, almost theoretical soiling at the time of operation makes much difference—it is a continuous leak from the anastomosis which kills and this does not occur in well-prepared defunctioned bowel. If resection and immediate anastomosis is made without a proximal colostomy then a leak would probably be fatal, whether there is an intestinal antiseptic in the faeces or no. Therefore, we rarely omit the temporary colostomy except in a few palliative resections of hopeless cases.

Cirrhosis of Liver. End-in-side Spleno-Renal Venous Anastomosis.—NORMAN C. TANNER, F.R.C.S.

C. G., male aged 61, a labourer.

History.—Heavy beer drinker in youth. Had pneumonia and malaria. In 1933 he had infective hepatitis. Since October 1947 he has suffered from central abdominal aching pain and the abdomen was getting bigger. In January 1948 the feet began to swell.

On examination.—A slender man, looking fairly well. Distended veins were seen coursing over the upper abdomen and round the umbilicus. There was marked ascites, and the liver was felt to be hard and knobbly.

Investigations.—X-rays of barium swallow and meal, and enema were normal. Blood: W.R. negative. Count normal. Blood proteins normal. Liver function tests: Blood alkaline phosphatase 10 units %. Takata-Ara reaction positive. Colloidal gold reaction negative. Thymol turbidity test negative (3 units).

The ascites made repeated paracentesis necessary.

Operation.—On March 10, 1948, under cyclopropane and curare. The patient was placed on his right side and a left transverse abdominal incision made, extending into the flank. There was some ascites, the liver was coarsely cirrhotic, the spleen hard and small. There was gross hypertension in all the branches of the portal vein. The spleen was removed, the splenic vein mobilized, and an end-in-side anastomosis made between the splenic and left renal veins, using a Blakemore vitallium tube. The tension was removed from the anastomosis by suturing pancreas to kidney.

Post-operative course.—The patient was treated post-operatively with heparin and had a quiet convalescence, but still has some ascites.

Comment.—There are obvious advantages in the end-in-side operation in that nephrectomy is avoided and experimentally there is some evidence that the tendency to thrombosis is less. Technically this is more difficult than end-to-end union. The problem here is, has the anastomosis remained patent? X-ray shows the tube in position. There has been no hæmaturia, an intravenous pyelogram is normal, and there is no left varicocele.

Perineal Urethrostomy Preliminary to Retropubic Prostatectomy.—H. K. VERNON, M.S.

Patient aged 82. Admitted with retention of urine and intermittent fever.

12.3.48: Perineal urethrostomy.

31.3.48: Retropubic prostatectomy.

8.4.48: Both wounds healed and patient voiding urine easily.

The advantage of this method of preliminary drainage of the bladder, suggested by J. G. Sandrey,¹ is that it leaves the abdominal wall undisturbed for a rapid retropubic prostatectomy later. The retropubic is the operation of choice in the aged prostatic with a large adenoma, because healing is quicker and the patient can be sat out of bed immediately.

¹See Sect. Urol., *Proceedings*, November 1948.

Multiple Primary Colonic Malignancy.—E. NANSON, F.R.C.S.

Mrs. E. T., aged 56.

History.—Fifteen years ago resection of right side of colon with ileo-transverse colostomy, followed by deep X-ray therapy for carcinoma of caecum. Three months ago malaise, lassitude, loss of weight. Admitted to St. James' Hospital 14.2.47 complaining of diarrhoea for three days, with three stools per day containing bright red blood. On night of admission had a severe hæmorrhage *per rectum* of about half a pint of bright red blood.

On examination.—A pale cachectic and very ill-looking woman. T. 100.8°. P. 100/min. R. 22/min. Tongue pale and atrophic. Abdomen: Two right mid-paramedian scars, and an area of radiation pigmentation in right lower abdomen. A firm mobile, nodular, slightly tender mass in left iliac fossa. Sigmoidoscopy normal. Barium enema showed a filling defect in pelvic colon 3 in. long, consistent with neo plasm (see fig. 1).



FIG. 1.—Mrs. E. T. Barium enema showing double lesion, sigmoid colon. (Arrow, top left, indicates ileo-transverse colostomy.)

FIG. 2.—Mrs. E. T. Operation specimen of sigmoid colon showing two carcinomata.

Blood-count.—R.B.C. 2,900,000; Hb 44%; C.I. 0.75; W.B.C. 8,800 (polys. 60%, lymphos. 25%, monos. 15%).

Patient was prepared for operation with a high protein diet, transfusions and sulphasuxidine.

4.3.48: Operation by Mr. Tanner. Through an oblique left inguinal muscle-cutting incision the pelvic colon containing two separate stenosing carcinomata, each with its own group of lymphatic metastases, was resected by the Mikulicz technique. In order to improve the artery bare. The liver and pelvis were free of metastases.

11.3.48: A clamp to crush the spur of the colostomy was applied.

30.3.48: Colostomy closed by extraperitoneal method.

Following the resection of the growths the patient's general condition has remarkably improved, and she has made an uninterrupted convalescence.

Pathological findings.—The pelvic colon contained two ulcerating carcinomata, approximately 3 in. apart, each with its own group of metastases (see fig. 2). Histological report not yet available.

Points of special interest.—(1) The patient was not suffering from multiple polyposis yet she developed three distinct primary neoplasms of the colon—one singly and two synchronously. (2) There was no evidence of distant metastases. (3) A profuse hæmorrhage of half a pint *per rectum* is a relatively uncommon event in neoplasm of the large bowel. (4) Having had a previous ileo-transverse colostomy it was not possible to make a defunctioning transverse colostomy as is our usual practice preliminary to doing an excision of pelvic colon and end-to-end anastomosis. Therefore the Mikulicz technique had to be resorted to.

POSTSCRIPT.—Histological report: Two separate adenocarcinomata of colon, with normal intervening mucosa.—E. N.

Physical examination.—Very ill, apathetic and drowsy. Skin showed reddish brown isolated papules, linear lesions and almost black indurated areas.

Blood-pressure 120/65.

Blood: Hypochromic anaemia. Hb 46%; R.B.C. 2,630,000. Urine: Spec. gravity 1.006 (fixed), alb. +, sugar 0.

Blood chemistry: Calcium 9.8 mg. %; plasma phosphorus 8.4 mg. %; plasma phosphatase

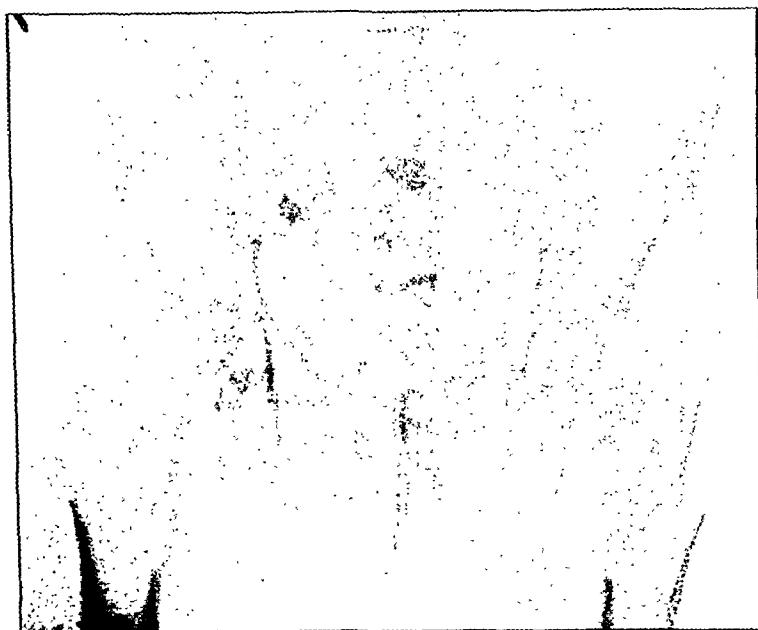


FIG. 1.

17.2 units; plasma proteins total 6.17%; fibrin 0.6%; albumin 2.94; globulin 2.63, blood urea 304 mg. %.

Radiological findings.—(1) Generalized osteoporosis. (2) Cortical thinning particularly of long bones, disintegration in the phalanges and especially in os pubis (fig. 1). (3) Widespread calcifications in the subcutaneous tissues (cf. fig. 3, p. 140¹). (4) Extensive arteriosclerosis of the arteries in hands and feet (fig. 2).

The patient died on November 22, 1944.

Post-mortem examination.—Chronic nephritis, marked enlargement of the parathyroids (only hypertrophy) (cf. fig. 2, p. 140²).

Comment.—The differential diagnosis between primary and secondary hyperparathyroidism in a patient with renal insufficiency may sometimes be difficult. Renal damage in primary hyperparathyroidism may be caused by precipitation of calcium in the renal pelvis, leading to calculus formation and pyelonephritis or by deposit of calcium within the kidney parenchyma. These calcifications can usually be recognized on X-ray examination and represent an important radiological sign for the diagnosis of primary hyperparathyroidism. The characteristic bone changes of osteitis fibrosa cystica are usually present, and examination of the blood chemistry revealing raised serum calcium and low phosphorus will in the majority of cases lead to a correct diagnosis.

¹*Proc. R. Soc. Med.*, 1944, 38, p. 140, Plate I.

²*loc. cit.* p. 140, Plate I.

[May 12, 1948]

Calcified Intrathoracic Cyst (Old Interlobular Empyema).—IVOR LEWIS, M.S.

Mrs. V. K., aged 26, married. She was referred by the Tuberculosis Officer. There was little in the past history except measles as a child. A healthy-looking, cheerful young woman; no clubbing of the fingers and no abnormal physical signs in the lung.

B.S.R. 6 mm. in one hour.

Sputum: A few c.c. per day, yellow, showed no tubercle bacilli.

X-rays showed a calcified cyst of ovoid shape in the right lung field, rather posteriorly.



FIG. 1.—P.A. view.



FIG. 2.—R. lateral view.



FIG. 3.—Photograph of the calcified shell. Note the hole, where it communicated with a bronchus.

There were one or two cavities the size of marbles to be seen in some of the X-rays just below this cyst (figs. 1 and 2).

Casoni test negative.

W.B.C. 13,200. 53% polymorphs., 2% eosinophils.

(It transpired that her chest had been X-rayed by "mass radiography" two years ago, apparently without comment. The film, however, cannot be found.)

Subsequent operation revealed a calcified shell of an old interlobular empyema, with a hole from it into the lower lobe bronchus, near which there were two small cavities.

The specimen was dissected free (fig. 3).

Convalescence was uneventful.

Chronic Renal Insufficiency with Secondary Hyperparathyroidism.—A. ELKELES, M.D.

Female, aged 21, admitted to Ashridge E.M.S. Hospital, August 1944. Within the last two years became increasingly pale and breathless and lost 2 st. in weight; amenorrhœa, irritating skin conditions in axillæ, cubital fossæ, under the breasts, groins, anogenital region and upper thighs. (Case was shown by J. E. M. Wigley and D. Hunter at Dermatological Section on November 16, 1944.¹)

¹*Proc. R. Soc. Med.*, 1944, 38, 141.

Section of Endocrinology

President—L. R. BROSTER, O.B.E., M.Ch.

[April 28, 1948]

The Hypothalamus and Water Metabolism

By G. W. HARRIS, M.A., M.D. Cantab.

Lecturer in Physiology, Cambridge University

THE hypothalamus can influence water metabolism in several ways: by influencing sweating, vascular tone, respiration and by other means. Only the control exerted through the mediation of the pituitary gland will be considered. The terminology for the various divisions of the pituitary gland has been standardized by the "Association for Research in Nervous and Mental Diseases", and the nomenclature they suggested is given below and will be adopted here (*see also fig. 1*).

Adenohypophysis—Lobus glandularis—	{ Pars distalis (anterior lobe)	
	{ Pars tuberalis	
	{ Pars intermedia	} posterior lobe
Neurohypophysis—Lobus nervosus—	{ Infundibular process	
(neural lobe)		
Infundibulum	{ Infundibular stem	Neural stalk together with sheath of portions of lobus glandularis designated as hypophyseal stalk
(neural stalk)	{ Median eminence of tuber cinereum	

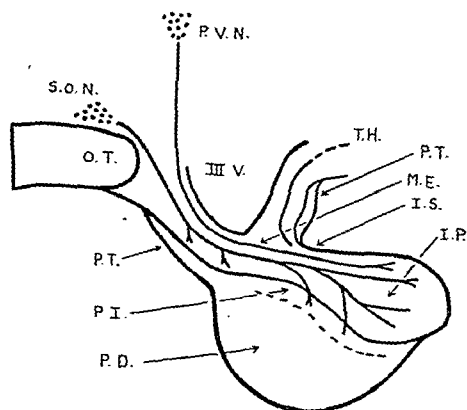


FIG. 1.—Diagram of a sagittal section through the hypothalamus and pituitary gland to illustrate the terminology used, and the nerve supply of the gland. The three parts of the neurohypophysis include the bulbous median eminence (M.E.), the constricted infundibular stem (I.S.) and the swollen infundibular process (I.P.). The adenohypophysis also consists of three divisions, the pars distalis (P.D.), the pars intermedia (P.I.) and the pars tuberalis (P.T.). It is established that the neurohypophysis is innervated by the supraoptic nucleus (S.O.N.) situated above the commencement of the optic tract (O.T.), and the paraventricular nucleus (P.V.N.) which is in intimate relationship with the third ventricle (III.V.). Other fibres constituting the tuberohypophyseal tract (T.H.) also run to the hypophysis, but their origin is unknown.

Anatomical connections between the hypothalamus and hypophysis.—There are two anatomical links between the hypothalamus and hypophysis; first a prominent nervous pathway, the hypothalamo-hypophyseal tract, which ends mainly in the neurohypophysis, and secondly a vascular connexion, the hypophyseal portal vessels, which connect with the adenohypophysis.

The case presented here shows the characteristic features of primary renal insufficiency with subsequent secondary hyperparathyroidism. In spite of advanced renal failure no metastatic calcium deposits in the kidneys are present, whereas calcification in the subcutaneous tissues and peripheral arteries is very pronounced. There is widespread osteoporosis and even some bone resorption with concomitant deposition of amorphous calcium; the bony changes, however, are in no way characteristic of osteitis fibrosa cystica. Furthermore the investigation of the blood chemistry reveals a considerable retention of non-protein nitrogen, a normal serum calcium and a much raised plasma phosphorus. Thus renal insufficiency with retention of urea was associated with a rise of phosphorus in the blood. Since renal excretion of phosphorus is related to the



FIG. 2.

activity of the parathyroid gland, it may be assumed that prolonged retention of phosphorus causes hyperactivity of the parathyroid in an attempt to eliminate the excess of phosphorus by an intensified phosphaturia. Not only is this compensatory hyperactivity of the parathyroid without lasting effect in cases in which renal damage is permanent and even progressive, but is responsible, in addition, for the mobilization of calcium from the skeletal system, resulting in general osteoporosis and precipitation of calcium in the subcutaneous tissues and arteries.

years that clinical diabetes insipidus may be controlled by the administration of posterior pituitary extract. Fisher, Ingram and Ranson (1938) have shown that the essential lesion in experimentally produced diabetes insipidus is one that interrupts bilaterally the supraoptico-hypophysial (S.O.H.) tracts. This is followed by atrophy of the neurohypophysis, failure in production of the antidiuretic hormone and diminished reabsorption of water by the tubules of the kidney. The converse experiment of stimulating the S.O.H. tracts with consequent liberation of the antidiuretic hormone and inhibition of a water diuresis requires a specialized technique for anaesthesia itself inhibits a water diuresis.

In order to stimulate the hypothalamus and pituitary gland in the unanaesthetized rabbit the remote control method has been used (Harris, 1947a). A small (secondary) coil is buried beneath the scalp and from this coil an insulated electrode passes through a small trephine hole in the skull to the desired region. (Such preparations may remain in a satisfactory condition for several years.) Stimulation is produced by placing the animal's head in the electromagnetic field of an external (primary) coil, the desired voltage being induced through the healed skin. Spread of the stimulus is not more than 0.5 mm. for the fibres in the neural stalk. In order to study the effects of stimuli administered to various parts of the hypothalamus and pituitary gland on a water diuresis the routine procedure is as follows:

Water is administered by stomach tube to a rabbit bearing an implanted coil, and the urine collected and measured every 15 minutes. When the urine flow has increased to 10 c.c./15 min. or more, the animal is stimulated, usually for a period of 1 minute. If the electrode tip is in, or in contact with, the S.O.H. tract in the median eminence, infundibular stem or infundibular process, a marked antidiuresis follows stimulation. The strength of the stimulus can be varied by varying the distance between the primary coil, held over the animal's head, and the implanted secondary coil. The amount of antidiuretic hormone liberated varies directly with the strength of the stimulus as shown by the extent and duration of the antidiuresis elicited. With strong stimuli the urine flow may be depressed to very low levels for several hours, though it rises eventually as the effect of the post-pituitary secretion wears off and the high water load is excreted. All intermediate grades of response may be obtained at will by varying the strength of the stimulus. In any one animal the antidiuresis evoked by a given stimulus remains constant over a series of days or weeks. The antidiuretic response following stimulation of the S.O.H. tract is similar qualitatively and quantitatively to that following the intravenous injection of an appropriate dose of post-pituitary extract. Control experiments have shown that if the electrode is within 0.5 mm. of the S.O.H. tract but not in contact with it, stimulation elicits a lessened antidiuretic response, but if the electrode is farther from the tract than 0.5 mm. (either above, below or lateral) then the diuresis continues unabated in spite of stimulation. These, and other, facts show that the stimulus used is very localized, and that the response is due to liberation of the antidiuretic hormone from the neurohypophysis by stimulation of the S.O.H. tract.

It is impossible to measure directly the amount of antidiuretic hormone liberated from the neurohypophysis by maximal stimuli, for the antidiuresis so produced is outside the range which can be assayed with any degree of accuracy. It has been found, however, that small amounts of antidiuretic substance are excreted in the urine following stimulation of the S.O.H. tract (Harris, 1948a). By comparing these amounts with those excreted after the intravenous injection of different doses of post-pituitary extract, and assuming that the secretion liberated from the neurohypophysis behaves in the same way in the blood stream as injected extract, the approximate figure has been obtained that stimulation of the S.O.H. tract for 1 minute liberates less than 50 mU. of antidiuretic hormone. This figure is in rough agreement with those obtained by entirely different methods, described below.

Post-pituitary extracts have many pharmacological activities and investigations have been made to see which of these activities follow stimulation of the S.O.H. tract. It has been found that such stimulation causes the secretion of substances which raise the relative (and sometimes absolute) chloride excretion in the urine, causes contraction of the oestrous or oestrogenized uterus, produces an increase in intestinal peristalsis, but has no effect on blood sugar and causes only slight rises in blood-pressure (Harris, 1947a, 1948b).

It is well known that posterior pituitary extracts may be separated into two fractions, a pressor and an oxytocic fraction. In the rabbit the pressor substance is responsible for the rise in blood-pressure, the antidiuresis and chloruresis, the increase in intestinal peristalsis and the hyperglycemia that follow injection of post-pituitary extracts, and the oxytocic substance for any uterine contraction which may follow such injection. In most whole extracts these activities are present in a constant proportion, that is, the ratio of oxytocic to pressor substance is constant. It seemed of interest then to see whether the

The hypothalamo-hypophysial tract starts in various hypothalamic nuclei. The origin of fibres in the supraoptic and paraventricular nuclei is established, but which of the other hypothalamic nuclei contribute fibres to the tract is doubtful though the anterior hypothalamic, ventromedial hypothalamic and more caudal nuclei have been suggested. The similar connexion of the supraoptic and paraventricular nuclei is of interest in view of their common phylogenetic origin and cytological and vascular architecture. The normal appearance of cells in these nuclei is similar to that of cells in other parts of the nervous system undergoing chromatolysis, that is, they have a peripheral distribution of Nissl substance, a clear perinuclear zone and an eccentric nucleus. Also both nuclei are exceedingly vascular. The number of cells in each supraoptic nucleus has been estimated at 7,000 (rat) and 60,000 (man), and the number of fibres in the supraoptico-hypophysial tract at 10,000 (rat) and 100,000 (man) (Rasmussen, 1940). The great majority of fibres of the hypothalamo-hypophysial tract end in the three subdivisions of the neurohypophysis, only a very few passing forwards into the pars intermedia. The exact mode of termination is doubtful, though most workers agree that a large number of fibres terminate as perivascular endings especially in the region of the median eminence. It is not possible at the moment to describe a secreto-motor ending for these fibres.

The hypophysial portal vessels were first described by Popa and Fielding (1930, 1933), and later by Wislocki and King (1936), and by Green and Harris (1947). The anatomy of these structures is now fairly clear (fig. 2). Small twigs of the internal carotid arteries supply a vascular plexus situated between the pars tuberalis and the median eminence, and from this plexus "vascular tufts" or "sinusoidal loops" penetrate the tissue of the median eminence. These loops are then in intimate contact with the wealth of nerve fibres in this situation. From these vessels the blood is drained into large portal trunks which pass to the pars distalis where they break up into the sinusoids of this part of the gland. Therefore at one end the wide trunks are continuous with the loops in the median eminence and at the other end with the sinusoids of the pars distalis, that is they are truly portal vessels. This system of vessels, with minor variations in pattern, has been found in all vertebrates so far examined from amphibians to man (Green, 1948*a*). Even in the porpoise, where the infundibular process is separated from the pars distalis by a thick dural septum, a typical and well-marked portal system exists (Harris, 1947*b*). The direction of blood-flow in these vessels has been the subject of much controversy, but has now been directly observed (under the microscope) in anaesthetized frogs (Green, 1947) and rats (Green and Harris, 1948) as being from the median eminence to the pars distalis. The exact vascular pattern varies amongst different mammals and seems to depend largely on the length of the pituitary stalk, for in dogs (with a very short stalk) the intermediate trunks of the vessels are abbreviated and the terminal capillaries and sinusoids approximated, whereas in man (with a long stalk) the vessels are elongated and very easily observed. Since the pars tuberalis has no proven endocrine function and since it bears a constant relationship to the sinusoidal vessels which penetrate the median eminence it has been suggested (Harris, 1947*c*) that the

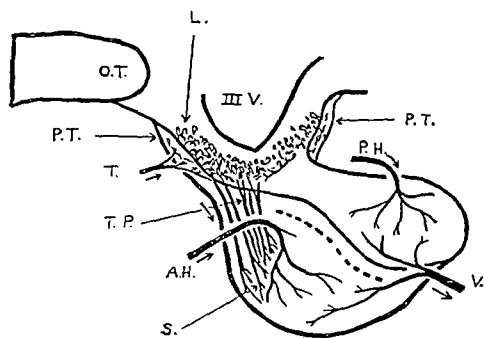


FIG. 2.—Diagram of a sagittal section through the hypothalamus and pituitary gland to illustrate the hypophysial vascular system. The details are more in accord with the organs of a rabbit, but the general plan is typical for mammals as a whole. Small twigs (T.) from the internal carotid arteries supply a vascular plexus situated between the pars tuberalis (P.T.) and the median eminence. From this plexus sinusoidal loops (L.), in large numbers, penetrate the tissue of the median eminence the blood from these loops being drained by the large portal trunks (T.P.) which eventually break up into the sinusoids of the pars distalis (S.). The pars distalis also receives a systemic arterial supply (A.H.) from the internal carotid artery, and the infundibular process a similar supply (P.H.) from the same source. The short veins into the surrounding venous sinuses

significance of the pars tuberalis lies in the fact that it forms a bed for the vascular pathway between the hypothalamus and pars distalis. (It may be mentioned that the two lobes of the pituitary also receive a systemic arterial supply from the internal carotid artery directly, and that their venous drainage passes by short wide veins to the adjacent venous sinuses—see fig. 2.)

The hypothalamus, neurohypophysis and water metabolism.—It has been known for many

abolishing the influence of the nervous system over the anterior pituitary. In keeping with these observations is the paucity of nerve fibres in this part of the gland.

There is, however, another anatomical pathway between the hypothalamus and anterior lobe of the pituitary gland, namely the hypophysial portal vessels described above. The hypothesis that the nervous system, and in particular the hypothalamus, controls the activity of the pars distalis (and so most of the other endocrine glands) through the mediation of the hypophysial portal vessels was suggested by Harris (1944) and restated with further anatomical data by Green and Harris (1947). It is possible that hypothalamic nerve fibres, ending on the upper set of capillaries in the median eminence, liberate some chemo-transmitter into the portal vessels which is carried humorally to the anterior pituitary and there controls or modifies the activity of this gland. Since this mode of control would involve a nervous and vascular link, it has been referred to as "neuro-vascular" control of the anterior pituitary. Evidence in favour of this view may be summarized as follows:

(1) Under normal conditions ovulation in the rabbit only occurs ten hours after coitus. This reaction has been analysed and found to involve reflex nervous stimulation of the anterior pituitary to liberate gonadotrophic hormone which acts on the ovaries to produce follicular rupture. The pituitary secretion occupies the first hour following coitus, but since the nervous stimulus of mating takes only a few minutes, it may be that one phase in the reaction is a slow humoral excitation of the anterior pituitary.

(2) It has been shown that electrical stimulation of the tuber cinereum in the unanaesthetized rabbit, for as short a period as 3 minutes, may be followed by a full ovulatory response (Harris, 1948c). Direct stimulation of the pars distalis, pars intermedia or infundibular stem for periods up to $7\frac{1}{2}$ hours was not followed by ovulation. If the anterior pituitary is under humoral control via the portal vessels, and is devoid of a secretomotor nerve supply, it is possibly not excitable by electrical stimulation applied directly to the gland.

(3) Very varied results have been obtained by different workers after sectioning the pituitary stalk. The discordant nature of these results may be due to varying degrees of regeneration of the portal vessels. Such regeneration does occur in the rat (Harris, 1948f). Work in progress indicates that if this regeneration is prevented from occurring female rats enter into permanent anæstrum, which suggests cessation of pituitary gonadotrophic function.

(4) Dempsey (1939), Dey (1943) and Leininger and Ranson (1943) found that a greater disturbance of the œstrous cycle of guinea-pigs followed a lesion in the median eminence than after section of the pituitary stalk. A possible explanation is that the former lesion produces a complete irreparable denervation of the portal vessels, whilst the stalk section allows the possibility of vascular repair.

There is as yet little convincing evidence regarding the mechanism by which the portal vessels may regulate the activity of the adenohypophysis. Dr. J. D. Green has made the suggestion (private communication) that the influence of these vessels may be exerted by a simple vasodilatation or vasoconstriction, thus increasing or decreasing the total blood supply of the anterior pituitary gland. Regarding the possibility of a specific chemotransmitter passing via the portal vessels from the median eminence to the pars distalis, two suggestions have been put forward. Taubenhaus and Soskin (1941) suggested a cholinergic transmission, as they obtained a pseudopregnancy response in rats in which a prostigmine-acetylcholine mixture had been directly applied to the rats' pituitary glands. Markee, Sawyer and Hollinshead (1947) obtained ovulation in rabbits after injecting dilute adrenaline directly into their pituitary glands and also showed that dibenamine (a sympatholytic drug) was effective in blocking ovulation following coitus in the rabbit (Sawyer, Markee and Hollinshead, 1947). They suggested, therefore, that the anterior pituitary is stimulated by an adrenaline-like substance which is humorally conducted to the gland.

Clinical observations correlated with post-mortem examination of the hypophysial vessels in patients with lesions involving these structures would be of great value. For example, it would be of interest to know the state of the portal vessels in a case such as that of Dandy's (1940) in which the pituitary stalk of a young woman was sectioned. This patient subsequently showed a mild diabetes insipidus together with normal menstrual cycles, pregnancy and lactation. The diabetes insipidus was doubtless due to atrophy of the neurohypophysis, but it is important to know whether, in such cases, the normally functioning anterior pituitary gland can be correlated with regeneration of the portal vessels. For a description of the hypophysial stalk in man, see Green (1948b).

secretion of the gland, elicited by stimulation of the S.O.H. tracts, had the same ratio of oxytocic to pressor activity as the extracts. This problem was investigated by the following methods.

(1) Simultaneous measurement of pressor (antidiuretic) and oxytocic activities. A weak stimulus was administered to the S.O.H. tract in a rabbit in which a uterine fistula had been prepared some time previously. The antidiuretic and oxytocic responses to this stimulus were measured and compared quantitatively with similar responses following intravenous injection of post-pituitary extract. Only one experiment was performed on any one day, but over a series of days a series of responses were obtained for comparison. It was found that stimulation caused a secretion which possessed less antidiuretic, in proportion to oxytocic activity, as compared with various post-pituitary extracts (Harris, 1947a).

(2) Concurrent measurement of pressor and oxytocic activities. Stimulation of the S.O.H. tract for 1 minute, has been shown to produce an oxytocic effect equivalent to 200–500 mU. of whole posterior lobe extract. Similar stimulation of the same animals, on a different day, was found to produce an effect on intestinal peristalsis and on the blood-pressure less than that elicited by 100 mU. of posterior lobe extract. Thus similar stimuli cause the secretion of more oxytocic substance than pressor (Harris, 1948b).

(3) The qualitative response of the uterus. The uterine movements of the conscious rabbit were recorded by means of a fistula through the abdominal wall. Intravenous injection of whole posterior lobe extract produces a marked uterine contraction (proportional to the oxytocic content of the extract) followed by an inhibitory phase (related to the pressor content). Thus the single uterine recording gives an approximate measure of both oxytocic and pressor activity of an extract or secretion. On this basis it has been shown that stimulation of the S.O.H. tract for 1 minute produces a secretion equivalent (in action on the uterus) to a mixture of, approximately, 250 mU. oxytocic substance and 50–100 mU. of pressor substance (Harris, 1948b).

Thus all the evidence obtained from experiments on unanaesthetized rabbits indicates that the secretion of the gland contains less pressor activity, relative to oxytocic, than is present in various standard extracts. For this reason it has been suggested (Harris, 1948d) "... that in replacement therapy during labour the purified oxytocic fraction be used instead of whole posterior-lobe extracts. However, more direct evidence on the reactions of the human uterus *in situ* to such extracts is desirable".

The hypothalamus, adenohypophysis and water metabolism.—The von Hann-Richter hypothesis states that a maximum diabetes insipidus only occurs in the presence of some normally functioning anterior pituitary tissue. It would seem that there is normally a balance between the specific antidiuretic action of the neurohypophysis and a diuretic influence of the adenohypophysis. It is possible that the pars distalis stimulates water excretion by an action on general metabolism, or indirectly through the thyroid or adrenal cortex, or by some unknown means. The above hypothesis offers an explanation for the clinical cases where a progressive lesion destroys first the neurohypophysis with the onset of diabetes insipidus, whilst further increase in the lesion with destruction of the adenohypophysis leads to regression of the diabetes insipidus.

There is much evidence (Harris, 1948e) that the secretion of the anterior lobe is under the control of the nervous system. As examples of such an influence may be quoted the cases of sexual precocity in young children associated with small localized hypothalamic tumours, the effect of light on the sexual rhythm of many mammals, the disturbances of the menstrual rhythm and lactation caused by emotional upsets, and the histological changes that are known to occur in the thyroid and adrenal cortex in association with changes in environmental temperature. All these reactions, and many others, are most easily explained on the assumption that the nervous system controls the output of the eutrophic pituitary hormones and thus indirectly the activity of the thyroid, adrenal cortex, gonads and breasts. It would appear teleologically probable then that the diuretic processes of the adenohypophysis are integrated with the antidiuretic processes of the neurohypophysis and the hypothalamus.

The question of nervous control of the anterior lobe of the pituitary (and so indirectly the thyroid, adrenal cortex and gonads) is one of the fundamental problems of endocrinology to-day. There is no sound evidence that this gland possesses a secreto-motor nerve supply. Three nervous pathways to the anterior pituitary have been described—hypothalamic via the pituitary stalk, sympathetic via the cervical sympathetic and carotid plexus, and a supply via the petrosal nerves. Each of these pathways, however, has been cut without

Recently I have been investigating the effect of infusion of extract of the posterior lobe when the urine secretion has been increased by the administration of sodium chloride by stomach tube to the conscious dog. Following the administration of sodium chloride in solution hypertonic to the body fluids, the kidney secretes urine rich in chloride (usually about 0.28 molar) but neither the composition nor the volume of the urine is affected by the infusion of extract of the posterior lobe at rates up to 15 micro-units per second. But after the administration of sodium chloride in solution approximately isotonic with the body fluids, the urine flow is usually about 2 ml. per minute, the concentration of chloride in the urine about 0.14 molar and the rate of excretion of chloride about 0.28 mg. equivs. per min. Now, an intravenous infusion of extract of the posterior lobe at about 4 micro-units per second reduces the urine volume to about 1 ml. per min., and increases the concentration of chloride in the urine to 0.28 molar; but the rate of elimination of chloride is unchanged during the period of the infusion. Even with faster rates of infusion of pituitary extract or following the administration of high concentrations of sodium chloride, the concentration of chloride in the urine of the dog under these conditions does not rise higher than 0.28 to 0.3 molar, so that the maximal physiological response of the kidney is produced by the infusion of extract of the posterior lobe at the slow rate of 4 micro-units per second. In this instance, as in the inhibition of water diuresis, the action of the extract is to cause decreased excretion of water, without great change in the excretion of other urinary constituents; and it has already been stated that in these small doses the extract has no effect on the blood flow through the kidney. It is now accepted that the action of the extract on the kidney is to stimulate the reabsorption of water by the tubules, and, indeed, this is probably the only effect on the kidney of the active principle of the posterior lobe in amounts ordinarily liberated in life.

Diabetes insipidus.—The polyuria of diabetes insipidus, associated by pathologists with lesions in the region of the pituitary and hypothalamus, has been regarded as produced by diminished function of the neural lobe since the demonstration independently in 1913 by von den Velden and Farini that the polyuria can be controlled by the subcutaneous injection of extracts of the posterior lobe. For many years attempts to produce diabetes insipidus by operative lesions in experimental animals produced very doubtful results. This may be exemplified by the effect, now well established, of removal of the posterior lobe of the pituitary in dogs by an approach through the soft palate and sphenoid bone. On the days immediately following the operation the dogs drink freely, and the daily urine volume increases from the normal figure of about 200 ml. per day to about 2 litres per day; but then the daily urine volume falls and 2 to 3 weeks after operation is about 300 ml. per day, at which level the fluid exchange persists indefinitely. However, in 1935, Fisher, Ingram and Ranson described an operation which produced persistent diabetes insipidus in cats, consisting of the section of the supraoptico-hypophyseal tracts by electrolytic lesions placed in the hypothalamus by means of a stereotaxic instrument. Subsequent post-mortem examination showed that when the lesions failed to interrupt the supraoptico-hypophyseal tracts no persistent polyuria followed; but in animals in which the tracts were sectioned, the daily urine volume for many months after operation was 300 to 400 ml. per day and the specific gravity of the urine 1.006 to 1.008, instead of the 100 ml. per day (sp. gr. 1.028 or more) of normal cats. Injection of extract of the posterior lobe reduced the daily urine volume of the diabetic cats to 100-170 ml. (sp. gr. 1.015 to 1.027). Despite differences in the configuration of the pituitary stalk, section of the supraoptico-hypophyseal tracts has also been shown to produce diabetes insipidus in the rat and the monkey; and in common with many others, I have observed diabetes insipidus in dogs in which the tracts have been cut by a stab wound in the floor of the hypothalamus between the optic chiasma and the pituitary. At post-mortem, there is always degeneration of the neurohypophysis. The pars nervosa and pituitary stalk distal to the lesion are found to be devoid of nerve fibres and shrunken, while extracts of the posterior lobe lack antidiuretic activity (Fisher and Ingram, 1936). Thus, the diabetes insipidus produced by the procedure of Fisher, Ingram and Ranson (1935, 1938) is adequately explained by the loss of function of the neurohypophysis, absence of the antidiuretic hormone from the circulating blood, and consequent reduced reabsorption of water in the renal tubules. Explanation may also be offered for the failure of other operative procedures to produce permanent diabetes insipidus. In the procedure of Fisher, Ingram and Ranson both the neural lobe and the pituitary stalk, which has many anatomical similarities to the neural lobe, are caused to degenerate; whereas after removal of the posterior lobe the pituitary stalk is left intact to form a possible source of the small amounts of antidiuretic hormone needed to restrain the urine flow to almost normal volume. Other operative procedures, despite adequate destruction of the neurohypophysis, cause extensive damage to the glandular parts of the pituitary, and polyuria may fail to appear because of loss of function of the anterior lobe. Of all operations described, that of section of the supraoptico-hypophyseal tract ensures the best conditions

In summary then it may be stated that the hypothalamus controls the neurohypophysis by means of the supraoptico-hypophysial tract, and that stimulation of this tract results in release of the antidiuretic hormone and inhibition of a water diuresis. As a working hypothesis it is suggested that the hypothalamus controls the adenohypophysis, and so various diuretic processes, by neuro-vascular transmission of stimuli through the hypophysial portal vessels.

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The Hypothalamus and Urine Secretion

By W. J. O'CONNOR

From The Department of Pharmacology, Cambridge University

Action on the kidney of extract of the posterior lobe of the pituitary.—Since the release of hormone from the neural lobe of the pituitary constitutes the only mechanism as yet established by which the hypothalamus can influence kidney function, special consideration must be given to the action of extract of the posterior lobe. One effect of the extract is well known: injected intravenously, it causes inhibition of water diuresis; or injected subcutaneously at the time of administration of water, it causes delay of the diuresis for several hours. Inhibition of water diuresis is brought about without change in the blood flow through the kidney (Cowan, Verney and Vogt, quoted by Verney, 1946). The amount of extract of the posterior lobe which need be injected is very small; in the dog, with which species most experimental work has been done, the intravenous injection of 1 milli-unit (0.0005 mg. of the standard powder) usually produces inhibition of water diuresis lasting five minutes; the intravenous infusion of the extract at a rate of 1 micro-unit per second (0.0000005 mg. of the standard powder) maintains the rate of urine secretion at resting level despite the previous administration of a diuretic dose of water. Emphasis has been placed on the minute amounts of the extract needed to inhibit water diuresis in the conscious animal because of the evidence to be presented later that such small amounts only are involved in the regulation of the activity of the kidneys, and also in order to avoid confusion with early experimental work with anaesthetized animals and using much larger doses of extract from which a diuretic action of extract of the posterior lobe was described. The antidiuretic action of extract of the posterior lobe is also exerted in diabetes insipidus in which condition, as in diuresis following the ingestion of water, there is a large volume of dilute urine.

Recently I have been investigating the effect of infusion of extract of the posterior lobe when the urine secretion has been increased by the administration of sodium chloride by stomach tube to the conscious dog. Following the administration of sodium chloride in solution hypertonic to the body fluids, the kidney secretes urine rich in chloride (usually about 0.28 molar) but neither the composition nor the volume of the urine is affected by the infusion of extract of the posterior lobe at rates up to 15 micro-units per second. But after the administration of sodium chloride in solution approximately isotonic with the body fluids, the urine flow is usually about 2 ml. per minute, the concentration of chloride in the urine about 0.14 molar and the rate of excretion of chloride about 0.28 mg. equivs. per min. Now, an intravenous infusion of extract of the posterior lobe at about 4 micro-units per second reduces the urine volume to about 1 ml. per min., and increases the concentration of chloride in the urine to 0.28 molar; but the rate of elimination of chloride is unchanged during the period of the infusion. Even with faster rates of infusion of pituitary extract or following the administration of high concentrations of sodium chloride, the concentration of chloride in the urine of the dog under these conditions does not rise higher than 0.28 to 0.3 molar, so that the maximal physiological response of the kidney is produced by the infusion of extract of the posterior lobe at the slow rate of 4 micro-units per second. In this instance, as in the inhibition of water diuresis, the action of the extract is to cause decreased excretion of water, without great change in the excretion of other urinary constituents; and it has already been stated that in these small doses the extract has no effect on the blood flow through the kidney. It is now accepted that the action of the extract on the kidney is to stimulate the reabsorption of water by the tubules, and, indeed, this is probably the only effect on the kidney of the active principle of the posterior lobe in amounts ordinarily liberated in life.

Diabetes insipidus.—The polyuria of diabetes insipidus, associated by pathologists with lesions in the region of the pituitary and hypothalamus, has been regarded as produced by diminished function of the neural lobe since the demonstration independently in 1913 by von den Velden and Farini that the polyuria can be controlled by the subcutaneous injection of extracts of the posterior lobe. For many years attempts to produce diabetes insipidus by operative lesions in experimental animals produced very doubtful results. This may be exemplified by the effect, now well established, of removal of the posterior lobe of the pituitary in dogs by an approach through the soft palate and sphenoid bone. On the days immediately following the operation the dogs drink freely, and the daily urine volume increases from the normal figure of about 200 ml. per day to about 2 litres per day; but then the daily urine volume falls and 2 to 3 weeks after operation is about 300 ml. per day, at which level the fluid exchange persists indefinitely. However, in 1935, Fisher, Ingram and Ranson described an operation which produced persistent diabetes insipidus in cats, consisting of the section of the supraoptico-hypophyseal tracts by electrolytic lesions placed in the hypothalamus by means of a stereotaxic instrument. Subsequent post-mortem examination showed that when the lesions failed to interrupt the supraoptico-hypophyseal tracts no persistent polyuria followed; but in animals in which the tracts were sectioned, the daily urine volume for many months after operation was 300 to 400 ml. per day and the specific gravity of the urine 1.006 to 1.008, instead of the 100 ml. per day (sp. gr. 1.028 or more) of normal cats. Injection of extract of the posterior lobe reduced the daily urine volume of the diabetic cats to 100-170 ml. (sp. gr. 1.015 to 1.027). Despite differences in the configuration of the pituitary stalk, section of the supraoptico-hypophyseal tracts has also been shown to produce diabetes insipidus in the rat and the monkey; and in common with many others, I have observed diabetes insipidus in dogs in which the tracts have been cut by a stab wound in the floor of the hypothalamus between the optic chiasma and the pituitary. At post-mortem, there is always degeneration of the neurohypophysis. The pars nervosa and pituitary stalk distal to the lesion are found to be devoid of nerve fibres and shrunken, while extracts of the posterior lobe lack antidiuretic activity (Fisher and Ingram, 1936). Thus, the diabetes insipidus produced by the procedure of Fisher, Ingram and Ranson (1935, 1938) is adequately explained by the loss of function of the neurohypophysis, absence of the antidiuretic hormone from the circulating blood, and consequent reduced reabsorption of water in the renal tubules. Explanation may also be offered for the failure of other operative procedures to produce permanent diabetes insipidus. In the procedure of Fisher, Ingram and Ranson both the neural lobe and the pituitary stalk, which has many anatomical similarities to the neural lobe, are caused to degenerate; whereas after removal of the posterior lobe the pituitary stalk is left intact to form a possible source of the small amounts of antidiuretic hormone needed to restrain the urine flow to almost normal volume. Other operative procedures, despite adequate destruction of the neurohypophysis, cause extensive damage to the glandular parts of the pituitary, and polyuria may fail to appear because of loss of function of the anterior lobe. Of all operations described, that of section of the supraoptico-hypophyseal tract ensures the best conditions

In summary then it may be stated that the hypothalamus controls the neurohypophysis by means of the supraoptico-hypophysial tract, and that stimulation of this tract results in release of the antidiuretic hormone and inhibition of a water diuresis. As a working hypothesis it is suggested that the hypothalamus controls the adenohypophysis, and so various diuretic processes, by neuro-vascular transmission of stimuli through the hypophysial portal vessels.

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The Hypothalamus and Urine Secretion

By W. J. O'CONNOR

From The Department of Pharmacology, Cambridge University

Action on the kidney of extract of the posterior lobe of the pituitary.—Since the release of hormone from the neural lobe of the pituitary constitutes the only mechanism as yet established by which the hypothalamus can influence kidney function, special consideration must be given to the action of extract of the posterior lobe. One effect of the extract is well known: injected intravenously, it causes inhibition of water diuresis; or injected subcutaneously at the time of administration of water, it causes delay of the diuresis for several hours. Inhibition of water diuresis is brought about without change in the blood flow through the kidney (Cowan, Verney and Vogt, quoted by Verney, 1946). The amount of extract of the posterior lobe which need be injected is very small; in the dog, with which species most experimental work has been done, the intravenous injection of 1 milli-unit (0.0005 mg. of the standard powder) usually produces inhibition of water diuresis lasting five minutes; the intravenous infusion of the extract at a rate of 1 micro-unit per second (0.0000005 mg. of the standard powder) maintains the rate of urine secretion at resting level despite the previous administration of a diuretic dose of water. Emphasis has been placed on the minute amounts of the extract needed to inhibit water diuresis in the conscious animal because of the evidence to be presented later that such small amounts only are involved in the regulation of the activity of the kidneys, and also in order to avoid confusion with early experimental work with anesthetized animals and using much larger doses of extract from which a diuretic action of extract of the posterior lobe was described. The antidiuretic action of extract of the posterior lobe is also exerted in diabetes insipidus in which condition, as in diuresis following the ingestion of water, there is a large volume of dilute urine.

Firstly, whether the salt be given in solution isotonic with or hypertonic to the body fluids, in normal animals or in animals diabetic after section of the supraoptico-hypophyseal tracts, administration of sodium chloride by stomach tube or by intravenous infusion causes increased rate of excretion of chloride in the urine. Thus the actual elimination of the salt is independent of the neurohypophysis; and, as already stated, is not altered by the intravenous infusion of extract of the posterior lobe of the pituitary. Secondly, when salt is given in hypertonic solution, but not when given in isotonic solution, the urine excreted is concentrated in respect of chloride; less water is lost from the body in the process of excretion of salt administered in hypertonic solution than when the same amount of salt is given in isotonic solution. But the chloride concentration of the urine remains low when salt is given in hypertonic solution to dogs diabetic following section of the supraoptico-hypophyseal tract. The experiments of Verney, together with the actions of the extract of the posterior lobe described at the beginning of this paper, provide the explanation. Salt in hypertonic solution causes an increase in osmotic pressure of the blood; which evokes from the neurohypophysis an increased output of hormone; which, reaching the kidney, stimulates the reabsorption of water in the renal tubules. Thus the urine is concentrated in respect of chloride and the salt is excreted with minimum loss of water, when given in hypertonic solution.

In the experiments of Verney (1947) not all crystalloids were equally effective in evoking the release of antidiuretic hormone, when injected into the common carotid artery in amounts calculated to give equal increases in osmotic pressure of the blood in that artery. Sodium chloride, sodium sulphate, and sucrose appeared to be equally effective; urea was without effect; and dextrose had intermediate activity, causing a release of antidiuretic hormone in the experiments first described using a rapid injection of high concentration, but not in the experiments with the slow infusion of lower concentrations. By demonstrating that previous ligation of the internal carotid artery greatly diminished the inhibition of water diuresis by the intracarotid injection of hypertonic solutions, Verney has established that the area sensitive to changes in osmotic pressure lies in the vascular bed of the internal carotid artery; and although no other proof is available, the peculiar anatomical features of the cells of the supraoptic nuclei, together with the large blood supply of the nuclei, suggest that these cells may themselves be the "osmoreceptors".

So we may picture "osmoreceptors" probably situated in the hypothalamus continually responding to the osmotic pressure of the circulating blood and causing in the dog the release of about 1 micro-unit per second of hormone from the neurohypophysis; if the osmotic pressure of the circulating blood decreases by 1% to 2%, stimulation of the "osmoreceptors", and so production of hormone by the neurohypophysis ceases, and water diuresis ensues; if the osmotic pressure rises, more hormone is released from the neurohypophysis and causes the kidney to secrete urine of maximum concentration. The mechanism is peculiarly adapted to maintain the osmotic pressure of the body fluids within narrow limits, and is comparable in its physiological aptness with the control of respiration by the action of carbon dioxide on the respiratory centre.

An output of hormone from the neurohypophysis can be excited by procedures other than changes in osmotic pressure. Emotional stress, induced in a dog during water diuresis, may cause inhibition of the urine flow; this inhibition is observed consistently with animals in which the kidneys and suprarenals have been denervated; resembles closely the inhibition by the intravenous injection of post-pituitary extract; and is practically abolished after removal of the posterior lobe of the pituitary (Rydin and Verney, 1938; O'Connor and Verney, 1942). The inhibition by emotional stress is thus due to release of antidiuretic hormone from the neurohypophysis during the emotion. Emotion produced by a variety of procedures is effective—the sounding of a motor horn, electrical stimulation to the flanks, running on a moving table, even the entry of a strange person into the room may evoke antidiuretic hormone and cause inhibition of water diuresis. Others have shown that acetyl-choline in the atropinized dog and nicotine injected intravenously may also cause inhibition of water diuresis due to release of antidiuretic substance from the neurohypophysis (Pickford, 1939; Burn, Truelove and Burn, 1945). O'Connor and Verney (1945), working with dogs with normal innervation of the kidneys and suprarenals, found that inhibition of water diuresis by emotional stress was by no means the rule. Of 21 normal bitches, the typical inhibition appeared consistently in only 3 and was not produced in any tests on 7; with the remaining 11 animals the typical inhibition appeared in some but not all tests of the effect of emotional stress. Most of these animals were then submitted to denervation of the kidneys and suprarenals, the operation consisting of the division of all visible nerve fibres in the renal pedicle, section of the splanchnic nerves, and removal of the second, third and fourth lumbar ganglia with the sympathetic chain between them. After this operation inhibition of water diuresis occurred with all animals in all tests of the effect of

for the production of polyuria of diabetes insipidus:—total loss of function of the neurohypophysis, without damage to the glandular parts of the pituitary.

The degeneration of the nerve fibres in the neurohypophysis distal to the site of section is accompanied by retrograde degeneration and ultimate disappearance of the cells of the supraoptic nucleus of the hypothalamus and so confirms that these are the cells of origin of non-medullated fibres of pituitary stalk. Similar degeneration occurs in the cells of the paraventricular nuclei (O'Connor, 1947a), indicating that some of the fibres of the stalk, perhaps one-sixth, arise from these cells. However, the peculiar features of the cells of the supraoptic nuclei are observed equally in the paraventricular nuclei, so that there appears to be no need to postulate separate functions for the two groups of cells and their axons in the neurohypophysis. Other neurones in the hypothalamus are not arranged in such compact cell masses as are the cells of the supraoptic and paraventricular nuclei, and so their degeneration following section of the stalk, even if it did occur, would be difficult to recognize; but only a few fibres other than those arising from the paraventricular and supraoptic nuclei pass down the pituitary stalk to the pars nervosa. In all probability, it is the processes of the cells of the supraoptic and paraventricular nuclei which form the link between the hypothalamus and the neural lobe of the pituitary. They probably determine the release of the antidiuretic hormone, and so provide the means by which the hypothalamus can influence the reabsorption of water in the renal tubules.

Factors determining the release of hormone from the neurohypophysis.—The recent work of Verney (1947) has developed experimentally the conception that the output of hormone from the neurohypophysis is determined by the osmotic pressure of the circulating blood. For these experiments, at preliminary aseptic operations, the common carotid arteries of dogs were enclosed in loops of skin so that, when the skin loops had healed, injections could be made into the circulation to the head repeatedly and without disturbance to the animal. The injection of hypertonic solutions of sodium chloride into one carotid artery during water-diuresis resulted in inhibition of urine flow: the inhibition followed a time course identical with that of the inhibition produced by the intravenous injection of a small dose of extract of the posterior lobe of the pituitary, and was reduced to about one-tenth in experiments after removal of the posterior lobe of the pituitary. Thus, a brief but large increase in the sodium chloride content of the blood reaching the head caused liberation of antidiuretic hormone from the neurohypophysis.

In further experiments (Verney, 1947) hypertonic solutions of sodium chloride were infused into one carotid artery at a rate chosen to cause an increase of about 2% in the osmotic pressure of the blood in that artery. The infusion was maintained for 40 minutes and during the infusion the rate of excretion of urine fell from the diuretic level of about 6 ml. per min. to 0.5 ml. per min., and slowly recovered when the infusion was stopped. Infusion of sodium chloride into a vein at the same rate did not inhibit the water-diuresis; but the fall in the rate of urine secretion during the intracarotid infusion could be matched by the inclusion in the intravenous infusion of sufficient extract of the posterior lobe of the pituitary to give a rate of infusion of 1 micro-unit per second. An increase of 2% in osmotic pressure of the blood in one carotid, then, caused the release of 1 micro-unit per second of antidiuretic hormone, and this sufficed to restrain the urine flow from diuretic to resting level.

These experiments enable explanation to be made of some features of the response of the dog to ingested water. Klisiecki, Pickford, Rothschild and Verney (1933) showed that when water was given by stomach tube to dogs, the water load of the tissues—that is the difference at any time between the volume of water absorbed from the intestine and the amount excreted in the urine—rose to a maximum 35 minutes after the administration of the water; but the rate of flow of urine reached its maximum 15 minutes later. The ingestion of 250–300 ml. of water in the dog causes a fall in osmotic pressure of the arterial blood of 1% to 2% and so (from the work of Verney just described) may be presumed to cause a fall of 1 micro-unit per second in the output of hormone from the neurohypophysis. In fact production of the hormone probably ceases, and as the hormone already in circulation is removed from the blood stream the urine flow increases to diuretic level; the lag between water load and rate of flow of urine is accounted for by the time needed to remove the hormone already in the circulation. Water diuresis, the response appropriate to a fall in osmotic pressure of the body fluids, appears to be determined by decreased activity of the neurohypophysis.

The neurohypophysis also determines an appropriate renal response to increased osmotic pressure of the circulating blood. In my own experiments it has become necessary to consider the changes in urine volume and composition which follow the administration of sodium chloride to dogs as composed of two independent responses of the kidney.

Section of Experimental Medicine and Therapeutics

President—Professor H. P. HIMSWORTH, M.D.

[April 13, 1948]

DISCUSSION ON STREPTOMYCIN

Professor Clifford Wilson discussed clinical trials of streptomycin in non-tuberculous infections: During the past twelve months these trials have been carried on at five London hospitals and eleven provincial centres. Owing to the comparative rarity of suitable cases, the wide range of conditions treated and the small quantities of streptomycin available, the investigation is still in the preliminary stage. The main effort has been directed against *H. influenzae* meningitis and has confirmed American experience that streptomycin is probably the most effective single therapeutic agent in this disease and that failures are almost entirely due to the rapid development of resistance to streptomycin. Encouraging results have been obtained with other forms of meningitis, and with septicæmia, urinary tract infections and local sepsis where these conditions are due to penicillin-resistant organisms, particularly *B. coli*, *Ps. pyocyanea* and *Proteus* (see also Wilson, C. (1948) *Lancet*, ii, 445).

Dr. Trevor P. Mann: *Streptomycin in treatment of tuberculous meningitis.*—During the last fourteen months we have studied and treated 33 cases of tuberculous meningitis at Hammersmith Hospital. In 32 the diagnosis was bacteriologically proven, and in the one remaining child the presumptive diagnosis was very strong.

Formerly, little was to be gained from the early recognition of the disease for there was no specific treatment and the patient was sure to die. To-day its detection in the prodromal stage, before the onset of neurological signs, has become an urgent necessity, for on the whole it is the early cases which derive most benefit from treatment. The possibility of meningeal involvement must always be considered in the known tuberculous child with unexplained symptoms. This group could in future provide a good source of early cases.

Diagnosis.—In hospital a positive or strongly presumptive diagnosis should be attained within twenty-four hours with prompt and unremitting investigation of a suspicious case. Full examination of the spinal fluid, radiography of the chest and a Mantoux test are part of an immediate and indispensable routine. A careful history is often a valuable guide in assessing the doubtful case. In half our patients there was evidence of close contact with tuberculosis. In all the children the Mantoux test was positive where this was carried out to a dilution of 1 : 100, and in just over half the cases the chest X-ray revealed pulmonary disease of a definite or suspicious nature. In 6 out of 7 cases showing milary infiltration of the lungs, choroidal tubercles were seen at the first examination and in one case tubercles were found in the absence of radiographic changes in the chest. The eye-grounds, therefore, must not be neglected.

The diagnostic importance of a low spinal fluid sugar content needs emphasis. In all except 3 cases the level was significantly lowered in the lumbar fluid at the first puncture, and in 3 patients with a high initial reading, serial punctures showed a progressively falling value. The chloride levels, on the other hand, were not significantly lowered in 13 of our 33 cases at the first examination. As far as the differential diagnosis is concerned, in children with a lymphocytic spinal fluid the possibilities usually rest between the several forms of meningitis of virus origin, tuberculous meningitis and possibly the serous tuberculous meningitis described recently by Lincoln (1947). Here, the chemistry of the fluid is of differential value. Serous meningitis, according to Lincoln, occurs not infrequently in children with active primary tuberculosis and clinically may closely simulate tuberculous meningitis. Spinal fluid examination offers the best means of differential diagnosis. In serous meningitis the pressure and number of cells may be increased but the chemistry of the fluid remains normal. Complete recovery is possible. MacGregor and Green, as long ago as 1937, reported 2 cases showing a similar syndrome where both cases recovered, their spinal fluid returning to normal. We have recently had a case which may be explained on this basis. A child of eighteen months was admitted in November 1947 with a tuberculous abscess of the left chest wall, and a provisional diagnosis of tuberculous meningitis. On admission there were no abnormal signs apart from irritability and the chest-wall swelling. Lumbar puncture showed a pleocytosis and fig. 1 portrays the C.S.F. findings over a period of three to four weeks. Because of the normal chemical values of her fluid on repeated

emotional stress. The explanation of this difference between normal and partially sympathectomized dogs was found to lie in an action of adrenaline on the neurohypophyseal mechanism. If, in a dog with kidneys and suprarenals denervated and so in which emotional stress always produced inhibition of water diuresis, emotion was induced immediately following an intravenous injection of a small dose of adrenaline, no inhibition of water diuresis ensued. Adrenaline did not modify the inhibition of water diuresis by injections of the extract of the posterior lobe of the pituitary, and so the conclusion was drawn that adrenaline, introduced by intravenous injection or set free from the animal's own suprarenals, may block the liberation of antidiuretic hormone from the neurohypophysis during emotional stress. The irregular appearance of inhibition by emotional stress in normal dogs thus found its explanation in the release of adrenaline from the suprarenals during the emotion.

The aspects of the relationship between the hypothalamus and urine secretion discussed in this communication have been dealt with at greater length in two lectures by Verney (1946, 1947) and in a review (O'Connor, 1947*b*), to which reference is recommended for further detail.

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punctures and the absence of neurological signs, streptomycin treatment was withheld. Her fluid returned to normal and she was discharged home in January of this year. She is well to-day. Culture and guinea-pig inoculation of the spinal fluid were negative.

The absence of tubercle bacilli in the stained smear does not exclude the diagnosis. Streptomycin must not be withheld for more than twenty-four hours when the other diagnostic elements provide strong presumptive evidence of tuberculous meningitis. However, adequate cultural and biological tests on pre-treatment specimens of the fluid are essential for later bacterial confirmation.

Treatment.—At first continuous intramuscular and intrathecal therapy was employed for long periods but it was soon noted that many patients derived benefit from interrupted treatment. In cases which were going to respond to streptomycin there was frequently a marked improvement in the mental state and general well-being during the rest periods, and where anorexia and vomiting, attributable to streptomycin, had been troublesome, this would usually cease. The trend of the C.S.F. elements during the rest period was often a useful prognostic guide when correlated with the clinical condition. For a short period the intramuscular route alone was used, but as our results were uniformly bad the method was soon abandoned. High streptomycin levels are obtained in the spinal fluid following intrathecal treatment (fig. 2) and concentrations of the order of 500 $\mu\text{g}/\text{ml}$. have been

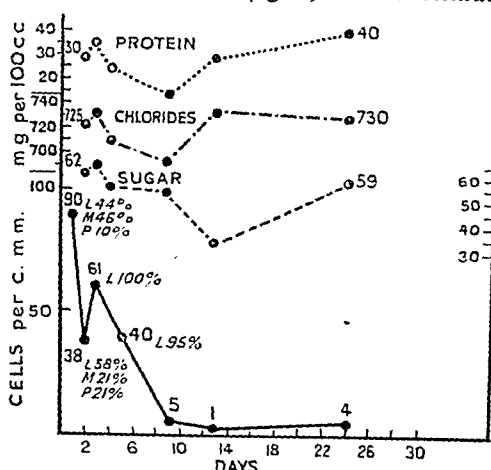


FIG. 1.

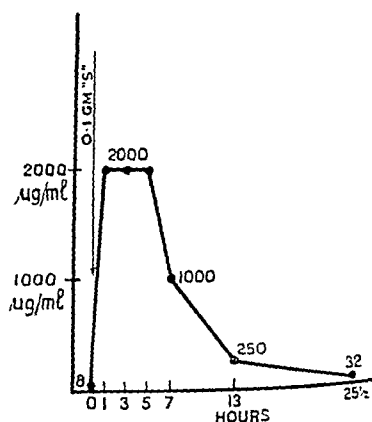


FIG. 2.

FIG. 1.—Patient T. P., aged 18 months. C.S.F. findings. L = Lymphocytes; M = Monocytes P = Polymorphs.

FIG. 2.—Patient G. H. Streptomycin levels in cerebrospinal fluid following intrathecal injection (0.1 gramme streptomycin).

found in the ventricles several hours after an intraspinal injection. Garrod (1948) has recently shown that high concentrations of streptomycin are rapidly bactericidal to the Oxford strain of *Staphylococcus aureus* if the size of the inoculum is not too large. His findings, if applicable to the tubercle bacillus, may afford a ready explanation for the undoubted benefit accruing from intrathecal injection.

Table I shows the scheme of treatment favoured at the moment. This is the least amount

TABLE I

Intra-muscular (12-hourly)	3/52	1/52	4/52	2/52	3/52
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Intramuscular "S" 0.02 gramme per lb. bodyweight per day.

Intrathecal "S" < 3 years 0.05 gramme in 4 c.c. saline.

> 3 years 0.1 gramme in 8 c.c. saline.

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recently the drug has been given six-hourly intramuscularly but there is experimental evidence to show that twelve-hourly administration is equally effective. If twelve-hourly injections are used we believe that treatment should be so spaced that the intrathecal injection is given approximately midway between the intramuscular injections, for we have found that after an intrathecal injection in several children off all treatment, streptomycin blood levels in the region of 4-8 $\mu\text{g/ml}$. are obtained in the six-hour period that follows. Giving the intramuscular treatment at 6 a.m. and 6 p.m. and the intrathecal injection at about midday we have found low but adequate blood concentrations during the night period. This level is maintained by a slow transference of the drug from the C.S.F. to the blood-stream. It is of interest to record that from 20% to 50% of the streptomycin given intrathecally is excreted in the urine during the following twenty-four hours.

SOME SIGNIFICANT TYPES OF CLINICAL RESPONSE TO TREATMENT

A third of our cases showed no response to streptomycin. In three cases, although rapid deterioration occurred shortly after starting treatment, life was prolonged for a number of months and the C.S.F. elements approached normal values. At autopsy, however, there was still evidence of active meningitis in these cases. The C.S.F. findings alone are not a reliable prognostic index.

Five of our cases have shown an immediate and uninterrupted improvement on treatment. Fig. 3 shows the C.S.F. values in one of our recovered cases both on and off streptomycin.

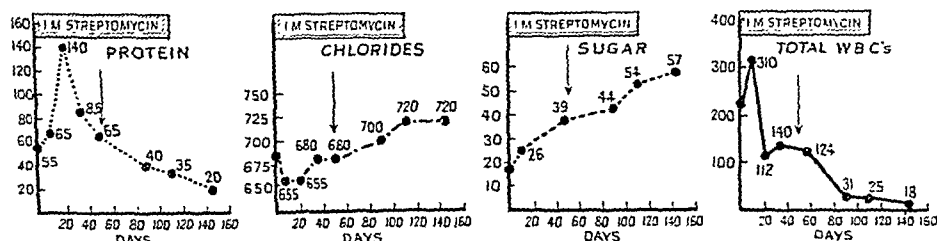


Fig. 3.—Patient J. C., aged 9 years. Cerebro-spinal fluid values in a recovered case, during and after streptomycin treatment. Arrows indicate cessation of intrathecal treatment.

Even on treatment the levels show a promising trend. Three months after admission there were no abnormal physical signs and the child was ambulant. Her good progress continues. Only when the clinical betterment is paralleled by a steady improvement in the C.S.F. elements can there be reason for optimism. In such cases one course of treatment, as outlined above, may suffice. When treatment has ended the patient must be closely watched for relapse and we feel that lumbar punctures should be done weekly until the fluid is normal, and subsequently at greater intervals.

This favourable type of response to treatment is unfortunately the exception; the one great hindrance to recovery, especially in cases showing a good initial response, is the development of a block at the level of the free margin of the tentorium. As a result of this occlusive process the normal flow of C.S.F. to the vertex is interrupted and hydrocephalus of a communicating type may result. Furthermore, streptomycin introduced from below is prevented from reaching the interpeduncular region in high concentrations, and it is here, as we know, that the maximal amount of exudate occurs in tuberculous meningitis. This stronghold of infection is probably the source of reinfection of the meninges in cases that relapse after an initial good response. Smith, Vollum and Cairns (1948) have recently demonstrated the presence of this block at the tentorial level by air studies in their patients, and we have confirmed their findings in a similar manner in several of our cases. Attempts have been made to attack this stronghold by the instillation of streptomycin through plastic tubes placed in the cisterna interpeduncularis. If this manoeuvre is to be successful, and technically it is quite feasible, it must be done if possible before the exudate in this region has become organized and impenetrable, in other words, during the early weeks of the illness.

TABLE II.—ANALYSIS OF RESULTS

Classification	Dead	Uncertain outcome	Recovered
Advanced cases, 15	13	1	1
Intermediate cases, 5	4	0	1
Early cases, 13	5	5	3
Total cases, 33	22	6	5

punctures and the absence of neurological signs, streptomycin treatment was withheld. Her fluid returned to normal and she was discharged home in January of this year. She is well to-day. Culture and guinea-pig inoculation of the spinal fluid were negative.

The absence of tubercle bacilli in the stained smear does not exclude the diagnosis. Streptomycin must not be withheld for more than twenty-four hours when the other diagnostic elements provide strong presumptive evidence of tuberculous meningitis. However, adequate cultural and biological tests on pre-treatment specimens of the fluid are essential for later bacterial confirmation.

Treatment.—At first continuous intramuscular and intrathecal therapy was employed for long periods but it was soon noted that many patients derived benefit from interrupted treatment. In cases which were going to respond to streptomycin there was frequently a marked improvement in the mental state and general well-being during the rest periods, and where anorexia and vomiting, attributable to streptomycin, had been troublesome, this would usually cease. The trend of the C.S.F. elements during the rest period was often a useful prognostic guide when correlated with the clinical condition. For a short period the intramuscular route alone was used, but as our results were uniformly bad the method was soon abandoned. High streptomycin levels are obtained in the spinal fluid following intrathecal treatment (fig. 2) and concentrations of the order of 500 $\mu\text{g}/\text{ml}$. have been

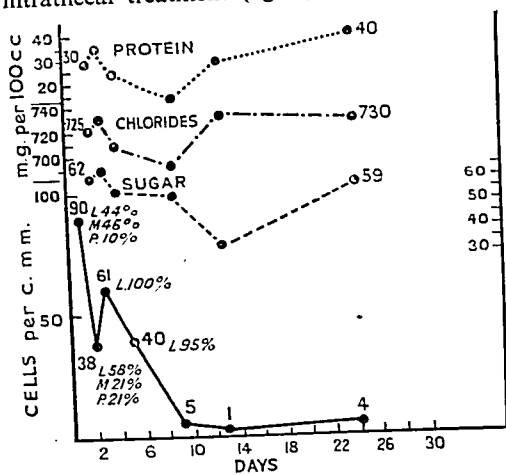


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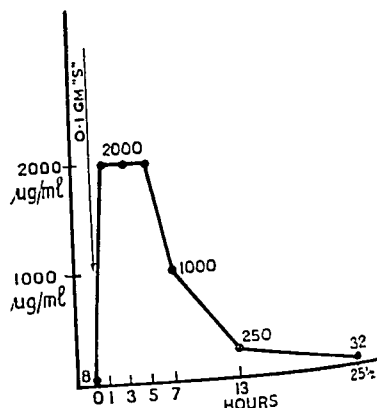


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Section of Obstetrics and Gynæcology

President—A. J. MCNAIR, F.R.C.S., F.R.C.O.G.

[March 19, 1948]

Spina Bifida Occulta and Nulliparous Prolapse. [Abstract]

By ARTHUR A. GEMMELL, M.C., T.D., F.R.C.O.G.

[This paper was prepared in conjunction with Dr. P. H. Whitaker of the Department of Radiology and Mr. R. L. Plackett of the Department of Applied Mathematics (Statistics) of the University of Liverpool.]

GENITAL prolapse is a condition commonly associated with the trauma caused by childbirth. It is, however, seen also in women who have not borne children. This group is variously called congenital or virginal or nulliparous prolapse. We prefer the term nulliparous as the condition occurs in childless women whether they are married or not. It is not present from birth and is therefore not properly described as congenital.

A number of cases of true congenital prolapse in newborn infants have been described and in nearly all these there was an associated lumbo-sacral spina bifida which proved fatal.

This knowledge led others before us to consider whether lesser defects of the posterior arches of the vertebræ, which might possibly involve the fibres of the fourth and fifth sacral nerves, could be associated with a weak pelvic floor.

An examination of the literature of the subject shows a conflict of opinion. This might be due to (1) An absence of clear indication of the parity of the patients. (2) Lack of definition of what the author means by spina bifida occulta. (3) Controls which, in our opinion, are not well chosen.

We, therefore, investigated the subject afresh and collected the following material:

(a) With the help of many colleagues all over the British Isles, to whom we express our thanks, we obtained X-rays of the sacrum and lower lumbar spine from 52 patients suffering from nulliparous prolapse, none of whom had, at the same time, an abdominal tumour.

(b) X-rays from a control group of 101 healthy nulliparous women (51 factory workers and 50 women medical students and nurses) all of whom declared themselves free from the following: (1) Motor weakness in the lower limbs or some segment of them. (2) Paræsthesia, or pain in corresponding zones, with loss of sensibility. (3) Defective sphincter control—e.g. nocturnal enuresis in adult life. (4) Abolition of tendon reflexes—knee or ankle.

In order to facilitate comparison and to provide groups of large enough size we made four groups, namely, non-closure of S5; 4 and 5; 3, 4, 5 or any other three segments and 2, 3, 4, 5 and any other four or all five segments. The results are:

	Non-closure of segments		Normals		Nulliparous prolapse
S5..	..	26	25.7%	10	19.2%
S4, 5	..	43	42.6%	19	36.5%
S3, 4, 5, &c.	..	25	24.7%	11	21.1%
S2, 3, 4, 5, &c.	..	6	5.9%	7	13.5%

At first glance these figures might suggest that there is a higher proportion of defects at the caudal end of the sacrum in the normal women and at the cephalad end in the prolapse patients but the series of differences between the groups has been tested by the χ^2 test which gives a value of 2.87. Consequently $P=0.4$, P being the probability that these or greater differences are due to chance. As P here is considerably greater than 0.05 there is so high a degree of chance that the differences have no significance.

The individual groups which appear to give the greatest differences are those with

Recovered Cases

I.—M. D. M. (Advanced). C.S.F. (April 1948) normal. Home and back at school. Slight (L) external rectus weakness. Normal mentality. Period of observation off treatment, 9 months.

II.—R. S. (Intermediate). (?) C.S.F. Receiving orthopaedic treatment for healing tuberculous osteitis of the left ischium at a convalescent home. Normal mentality. Period of observation off treatment, 9 months.

III.—B. A. (Early). C.S.F. (April 1948) biochemically normal: 20 lymphocytes. Mental and physical status normal. Period of observation off treatment, 6 months.

IV.—J. C. (Early). C.S.F. (April 1948) biochemically normal: 20 lymphocytes. Mental and physical status normal. Period of observation off treatment, 60 days.

V.—B. R. (Early). C.S.F. (April 1948) normal. Home and back at school. Mental and physical status normal.

POSTSCRIPT (October 1948).—All 5 recovered cases continue to make good progress. Cases II and IV now have a normal spinal fluid. The C.S.F. of Case III is normal except for 10 cells.

SUMMARY OF RESULTS

Five cases have recovered out of a total of 33 cases; 7 of the advanced cases were moribund on admission and died in the first week; 12 children were under 3 years of age and all have died; 3 cases are at this moment improving on treatment. A conservative estimate of the recovery rate is therefore 20% at the moment. The ultimate prognosis in the 5 cases classified as "recovered" will, of course, remain in doubt for some time. Psychometric tests performed on the 5 recovered children by Dr. Margaret Ferguson have shown them all to be normal.

I wish to express my gratitude to Dr. Dermot MacCarthy, and to Dr. Mary Barber and Dr. I. Doniach.

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Dr. J. Rubie: In a series of 50 cases of tuberculous meningitis treated at Highgate Hospital with streptomycin there are 21 surviving. These include 2 who have survived for more than 300 days, 4 more than 250 days, 2 more than 200 days and 1 more than 150 days. 6 have normal cerebrospinal fluid and 10 are clinically fully recovered. Two cases show slight ataxia and one of these two is deaf.

However, of the 29 who died, 8 died within seven days of admission and a further 14 cases received streptomycin by the intramuscular route only—a method now regarded as inadequate since only 2 of the cases thus treated recovered.

Failure is almost invariably due to the exudate causing mechanical obstruction to the circulation of the cerebrospinal fluid which in turn causes hydrocephalus. It is the hydrocephalus which causes death and it seems to be rather a matter of chance how soon it develops in the course of the disease. The hydrocephalus determines the stage of the disease and not the length of the history. It develops sooner in infants, and of the 50 cases, only one under 3 years of age survives and 14 under 3 years of age have died.

Our efforts must be directed to the prevention and treatment of the block—by early diagnosis and prompt treatment, and possibly by earlier surgical intervention such as ventricular drainage.

POSTSCRIPT.—The above figures were given in April 1948. The figures in October 1948 show that 8 of the above series have survived for more than one year and 11 have a normal cerebrospinal fluid.—J. R.

Dr. J. W. Crofton: The result of a course of streptomycin treatment for a case of pulmonary tuberculosis will probably depend on several factors. If the patient is left with large unclosed cavities, which cannot be controlled with collapse therapy, he will probably relapse, and this has occurred in at least two of our patients treated under the M.R.C. Scheme at the Brompton Hospital. The second factor is the development of streptomycin-resistance in the patient's tubercle bacilli. This is obviously important but its exact significance is yet to be assessed. It is possible that the present crude methods of testing for streptomycin resistance may show the development of resistant organisms when these, in fact, represent only a small proportion of the total population of tubercle bacilli in the patient. Streptomycin may therefore continue to attack the remaining susceptible organisms.

The third factor is, of course, the resistance of the patient which must take on where the streptomycin leaves off. The tubercle bacilli from most of our cases have developed streptomycin-resistance, yet many of the patients have continued to improve and some have become sputum-negative. Either the streptomycin maintained its effect on a significant residuum of susceptible tubercle bacilli, or the patient's powers of resistance were adequate to cope with the remaining infection.

fibroids, or even a carcinoma. The chief advantage of the operation is that when the uterus has been removed a very efficient fascial shelf can be reconstructed from the total depth of the broad ligament down to and including the utero-sacral ligament. The chief recommendation of this shelf is that by sewing the round ligaments together, and anchoring them to the triangular ligament, they form under the bladder neck a kind of Millin's sling, made of round ligament. The effect that this has upon stress incontinence is most beneficial.

Once a surgeon is used to this method he will find it easier to perform than Fothergill's operation. The great criticism of vaginal hysterectomy in the past has been its liability to produce a subsequent hernia of Douglas's pouch. In my small series, in which every case has been personally examined by me, I have found one such hernia, and I operated on it at once, so that I should have a clean bill to present to this Meeting. I have now altered the technique of the operation and direct special attention to the suturing of the utero-sacral ligaments across Douglas's pouch. With improved technique and greater experience, hernia here should become uncommon.

A film was shown by the author to illustrate his own technique.

Anæsthesia, post-operative care and results were then discussed, and the author continued: I should like to conclude with a plea for a bold surgical handling of all women with prolapse, regardless of their age. This is a most distressing and disabling condition, limiting the social activities of the citizen. The day of pill and pessary gynaecology is passed, and I am happy to say that I have inserted no rings or Napier's pessaries, or any other contrivance in the last two years. There is no more grateful, and no more rejuvenated person than the successfully operated upon prolapse patient and there is no more pathetic spectacle than the woman who has worn a ring for twenty or thirty years, with stress incontinence, which a ring never cures, and pessary ulceration and vaginitis, not to mention the possibility of a cancer developing from the ring. We should not, therefore, deny the benefit of surgery to any of these cases.

The following speakers also contributed to the Discussion:

Mr. V. B. Green-Armytage; Mr. Wilfred Shaw; Mr. Arthur Gemmell; Mr. Leslie Williams; Professor C. H. G. Macafee; Mr. William Hawke; Mr. A. J. Wrigley; Mr. Everard Williams; Mr. C. M. Gwillim.

[May 21, 1948]

Advanced Ovarian Pregnancy.—ARNOLD WALKER, F.R.C.S.

Mrs. I. Y., aged 38, was admitted to the Luton Maternity Hospital on May 16, 1946, at about 34 weeks with a history of severe abdominal pain for two or three days. She had had one previous pregnancy which was normal. The foetal heart was heard and the pain improved. About four weeks later, the foetal heart stopped and after waiting some ten days in the expectation that labour would start, laparotomy was performed.

On opening the abdomen, a large mass of necrotic tissue was found adherent to the abdominal wall. On passing the hand between the tumour and the parietal peritoneum, membranes were ruptured and a macerated foetus weighing 6 pounds 4 ounces was removed. The tumour separated with ease and was lifted out of the abdomen. It looked like a twisted ovarian cyst with a thrombosed but untwisted pedicle. It arose from the right side and the right tube could be seen stretched over the tumour. Around one circumference, the amniotic membrane was attached and this was stripped off the abdominal wall and abdominal organs with the greatest of ease. The pedicle was not more than 5 centimetres across with the ovarian ligament and ovario-pelvic fold clearly defined. When this pedicle had been tied and the tumour removed, the peritoneum which had been in relation to it appeared to be undamaged. The uterus, left tube and ovary were adherent but except for this the

non-closure of four or five segments in (a) the students, and (b) the prolapse patients—2 in 50 students and 7 in 52 prolapse patients, but even here using Fisher's exact test (which can be used for very small numbers) $P=0.09$ and so there is no significance in the difference especially as we have selected the group where it is greatest.

Thus the conclusion from this investigation is that there is no relationship between the occurrence of spina bifida occulta and that of nulliparous prolapse, where spina bifida occulta is used to mean non-closure of the posterior arches of the sacral vertebrae.

There remains one possibility which has not been examined during this investigation. It might be that the elements of the fourth and fifth sacral nerves, which supply the pelvic floor, are involved in different degree even where the defects in the sacral vertebrae have the same or similar appearances. This hypothesis could be tested by examining the muscular and sensory reactions of the structures supplied by these segments, but it seems unlikely since 5 in 52 prolapse patients show complete closure of the dorsal wall of the sacrum and the only individual with complete absence of the dorsal wall had no prolapse.

3. DISCUSSION ON THE ROLE OF VAGINAL HYSTERECTOMY IN TREATMENT OF PROLAPSE. [Abstract]

Mr. A. C. Palmer: About 1920, the idea took shape that some forms of prolapse require removal of the uterus in the attempt to rebuild the pelvic diaphragm. During the last twenty-five years, this idea has ripened into conviction.

It is interesting that the surgical treatment of prolapse is not yet standardized and that it lies somewhere near the frontier of gynaecological surgery. It does this, in spite of the fact that prolapse must be very nearly contemporary with the first labour. It remains true that men of great experience are not yet agreed on the best methods of obtaining a stable result.

My answer to the question, "What is the position of hysterectomy in the surgical treatment of prolapse?" can be summarized in three words: (1) Never, (2) Sometimes, and (3) Always. *Never* applies when prolapse is confined to the walls of the vagina; *Sometimes*, when the cervix is in the first stage of procidentia, i.e. when it has fallen to round about the vulval level; *Always*, when the cervix is outside the vulva.

The variations in treatment depend upon what has happened to the utero-sacral ligament. If the cervix has reached the vulva by stretching and without damage to the utero-sacral ligament, hysterectomy is contra-indicated. If on the other hand, the cervix has brought the utero-sacral ligament down to the vulva with it, so that the index finger can easily be hooked round the ligament, then I think hysterectomy is indicated. When the cervix is well outside the vulva, it must bring the utero-sacral ligament down with it and, in my opinion, is always an indication for hysterectomy. Removal of the uterus means that the utero-sacral ligaments are in fact shortened and, when approximated in the mid-line, stabilize the vault of the vagina. In my hands, infolding the ligaments below and in front of the cervical stump does not stabilize the vault of the vagina and too many of my cases have come back in a year or two, with the vagina again everted. After hysterectomy, only 3 out of 300 cases have returned with an enterocele and 1 with a cystocele. These were due to errors in judgment during the operation.

Mr. John Howkins: Though I am fully conscious of the value and efficiency of Fothergill's operation, and I am not proposing that Mayo's operation should replace this well-tested old friend, which has held the field in the hands of so many different surgeons, employing many different techniques, I would submit that the keystone doctrine is open to a fallacy. The vault of the vagina and the cardinal ligaments are not rigid structures, and do not give strength in compression as an arch does.

In removing the uterus, at or near the menopause, one frequently eradicates an organ which may be causing symptoms of excessive bleeding, which may harbour

(3) It is not uncommon to find a considerable reduction in plasma chlorides in anuric patients, in which case sufficient sodium chloride should be administered by mouth, either in tablet or capsule form or dissolved in the daily fluid allowance to return this level to normal. This may, however, prove impossible as the salt may cause vomiting. If any urine is being passed, the sodium chloride lost should be balanced by sodium chloride administered, similarly with vomiting. Where a chloride level is normal and there is no chloride loss, no salt whatever should be administered.

It is the rule to find a reduction in carbon-dioxide combining power of the plasma, but if the fluid balance and diet are carefully controlled this will not require any special attention. In cases in which the management has not been ideal and a severe acidosis is present, this can probably only be righted effectively by dialysis.

If a patient remains anuric, or virtually so as considered by urea output, six days after the onset of the acute renal failure, dialysis is undertaken with the artificial

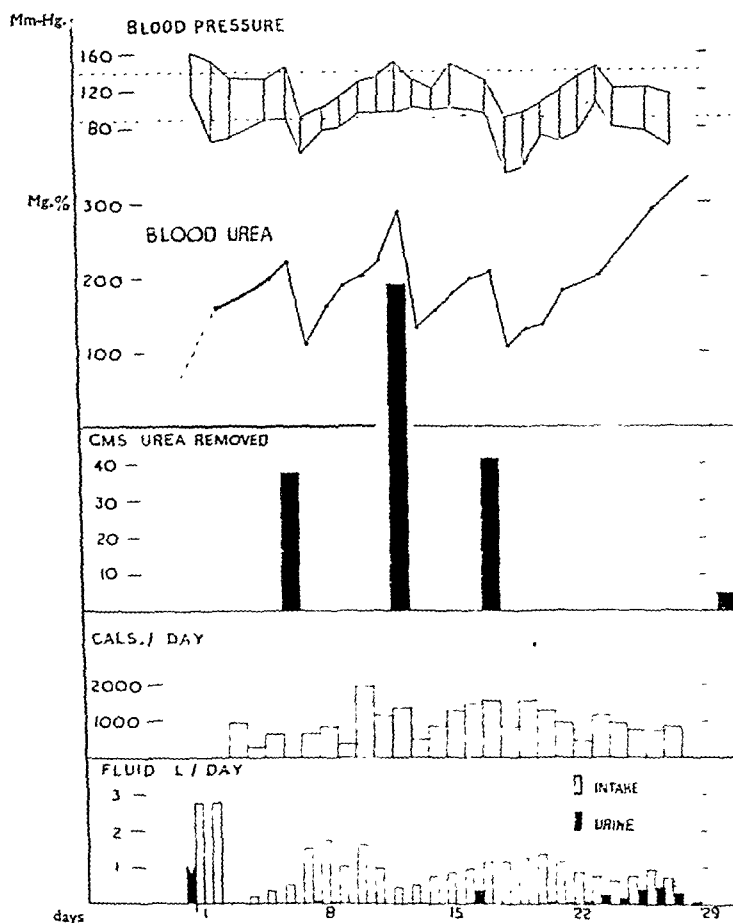


FIG. 1.—Urea removed: The three tall blocks represent grammes of urea removed by the "artificial kidney". Approximately 40 litres of blood were dialysed on each of the three occasions. The small block represents the total urea excreted by the kidneys in the twenty-eight days.

kidney in order to remove protein breakdown products and to right any electrolyte imbalance.

On the sixth day of anuria in this patient the blood urea had risen to 220 mg.%. Dialysis was performed and 38 grammes of urea removed and the blood urea reduced to 112 mg.%. On the twelfth day the blood urea had again risen, now to 290 mg.%, dialysis removed 88 grammes of urea and the blood level was reduced to

abdominal cavity was as clean as it is after the removal of a simple, pedunculated ovarian cyst. The tumour was roughly globular in shape and its diameter varied between 13 and 20 centimetres. Its surface was smooth and divided into two halves by the attachment of the amnion. From the foetal surface which bulged into the amniotic cavity, there arose a necrotic umbilical cord. On the smooth maternal surface could be seen the stretched-out fallopian tube which appeared to be intact.

The tumour was examined by Professor Willis and Dr. L. W. Proger at the Royal College of Surgeons but owing to its advanced state of necrosis it is not possible to identify even the limits of the placenta. From its anatomical relations the tumour clearly consists of the placenta and a right ovarian tumour.

It is believed that this is a primary ovarian pregnancy in an ovarian tumour sufficiently large to contain the pregnancy until the chorion had lost its invasive properties. At some stage, the bag of membranes must have herniated out of the tumour probably before the attack of pain which may have been due to hæmorrhage into the tumour.

Accidental Hæmorrhage with Bilateral Cortical Necrosis of the Kidneys, Treated by Artificial Kidney.—A. M. JOEKES, M.A., B.M., B.Ch., and G. M. BULL, M.R.C.P. (for GLADYS DODDS, F.R.C.S.).

The patient was a young married woman of 24; last menstrual period in 4th week of August 1947; expected date of delivery June 20, 1948. She was seen in January and February of this year in the Ante-Natal Clinic at the Mothers' Hospital, Clapton; B.P. 110/80 and no albumin in the urine was found.

9.3.48: Trace of albumin in the urine. B.P. 114/70, and Hb 60%. Treated with iron and liver injections as out-patient. 16.3.48: Urine: no albumin. B.P. 110/70.

31.3.48: Admitted 9 a.m. to Mothers' Hospital, Clapton, under the care of Dr. Gladys Dodds having vomited three times in the night and at 4 a.m. onset of acute abdominal pain with a small loss of blood *per vaginam*. The previous day she had felt perfectly well.

On examination.—Pale, face puffy, slight œdema of the ankles, B.P. 160/120. Uterus wood hard, tender, and the size of 36 weeks as opposed to actual 29 weeks. $\frac{1}{2}$ oz. of urine was obtained by catheter; this boiled solid with albumin. Diagnosis: Toxæmia of pregnancy with concealed accidental hæmorrhage.

The same afternoon normal delivery occurred of a stillborn fœtus; the placenta was expelled with a large retro-placental clot. After delivery B.P. 150/100. No urine was obtained on catheterization.

1.4.48 and 2.4.48: B.P. 150/100. No urine obtained on catheterization.

With a diagnosis of bilateral cortical necrosis she was at once transferred to the Hammersmith Hospital for treatment by blood dialysis with the "artificial kidney" [1] if anuria persisted.

The subsequent course of events can be seen from the chart. The total urinary output in the twenty-nine days that the patient survived from the start of anuria amounted to less than 2 litres. The urea concentration in the urine was less than 300 mg.% and the total amount of urea excreted by the kidneys in the twenty-eight days was only 5 grammes.

The treatment of anuria or oliguria can be divided into three main headings: (1) Fluid balance. (2) Diet. (3) The maintenance of or correction of an abnormal to a normal electrolyte pattern.

(1) *Fluid balance.*—The total fluid intake by any route intravenous, rectal or oral is maintained at 1,200 to 1,500 c.c. per day in excess of fluid loss in urine and vomit.

(2) *Diet.*—An intake of 2,000 calories per day is aimed at, with a minimal protein content. This diet is extremely difficult to administer successfully owing to the unpalatable food that the restricted choice permits; those that are available are fat in the form of margarine, carbohydrate as cane sugar, glucose or lactose and fruit. Borst [2] has described in some detail the diet as he uses it.

Section of Odontology

President—HUMPHREY HUMPHREYS, O.B.E., M.C., M.B., F.D.S.

[April 26, 1948]

Experimental Investigation Into Factors Concerning the Growth of Cysts of the Jaws

By P. A. TOLLER, L.D.S.

INTRACYSTIC PRESSURE

THERE is much evidence to suggest that certain cysts increase in size by reason of the fluid tension within them. This was recognized early by the French and German surgeons after the discovery that opening a cyst into the mouth checked further growth and subsequently led to a decrease in size of the tumour. Cysts occurring between the roots of teeth cause these roots to be displaced apart as if by pressure (cases quoted by Potts, 1927). Another observation concerns the migration of teeth associated with dentigerous cysts. Included teeth are frequently found lying at relatively great distances from their sites of development. These occurrences are strongly suggestive of a pressure effect, since if the growth of the cyst had simply been due to the proliferation of tumour cells then it would be expected that the tooth would remain static in relation to the bone and the tumour would grow around and pass it.

An interesting point to notice is that teeth included in dentigerous cysts appear to be moved by forces acting on the crown and its epithelial attachment. Collected cases and reports of cases show that cementum is not exposed in a cyst cavity even when cysts are in long-standing contact with tooth roots. Slow absorption of roots sometimes occurs. These facts tend to argue that simple pressure largely effects the expansion of a cyst.

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The disadvantage of this apparatus is that a manometer tube of at least one meter in length is needed, which is manageable in a laboratory but not in the ward or operating theatre. Mercury manometer or simple aneroid types were not considered sufficiently accurate although both have occasionally been used for the sake of convenience.

The size of the exploring cannula had to be selected carefully for several reasons: (a) The semi-fluid contents of some cysts tend to choke a narrow cannula; (b) a wide cannula has a lacerating effect on the tissue as it is inserted and a minute escape of fluid might result. A wide cannula would also have a disturbing effect on the volume of a small cyst, especially if it had to be passed through bone; (c) a narrow bore tube results in increasing the inertia of a hydrostatic system, by reason of the "drag effect" varying as a function of the diameter of the bore.

130 mg. % of urea. On the seventeenth day the blood urea had again risen to 210 mg. %, dialysis removed 42 grammes of urea and the blood level was reduced to 110 mg. urea %.

After the third dialysis the patient remained relatively well for several days and a period of over three weeks had elapsed since the original renal catastrophe. It was decided that while the diagnosis of cortical necrosis was almost certainly correct, were there sufficient kidney tissue surviving to keep the patient alive a considerable diuresis would by this time have been expected. In view of the very small amounts of urine and extremely poor urea concentration, it was not felt justifiable to try to maintain this patient's life yet further by means of the artificial kidney, the more so as one could only give a virtually hopeless prognosis to the young husband.

The patient died on the twenty-eighth day and a post-mortem confirmed the diagnosis of bilateral cortical necrosis. Typically the naked-eye appearance of a longitudinal section of the kidney showed sparing of a thin rind of subcapsular tissue and a rather wider juxtamedullary zone. The histological examination showed tubules but no glomeruli in the subcapsular zone, a fairly large number of surviving glomeruli in the juxtamedullary zone but the majority of the accompanying tubules, however, were dilated and had debased epithelium¹.

That it had been possible to maintain a patient's life for twenty-eight days in the absence of any significant renal function would seem to justify the claim that the artificial kidney is an effective treatment for acute uræmia, and should enable us to tide over a patient during the crucial time that the kidneys might be recovering from an acute catastrophe.

REFERENCES

- 1 KOLFF, W. J. (1946) *The Artificial Kidney*. Kampen; (1947) *New Ways of Treating Uræmia*. London.
- 2 BORST, J. G. (1947) *Ned. Tijdschr. Geneesk.*, **91**, 2718.

The following specimens were also shown:

- (1) Endometrioma of Cæcum with Mucocoele of Appendix. (2) Cervical Polyp.
- (3) Ovarian Cyst.—Dr. J. BAMFORTH.

Unusual Foreign Body in a Pregnant Cervix.—Miss JOSEPHINE BARNES.

Renal Cortical Necrosis.—Dr. J. F. HEGGIE and Dr. A. W. PURDIE.

Pelvic Splenule.—Mr. ANTHONY CHARLES.

Primary Ovarian Krukenberg Tumour.—Miss DOREEN DALEY.

- (1) Broad Ligament Tumour. ? Diagnosis. (2) Malignant Melanotic Ovarian Tumours.—Dr. MAGNUS HAINES.

- (1) Carcinoma of Cervix in a Procidencia. (2) Mesonephroma of the Ovary.—Mr. WILLIAM HAWKSWORTH.

Fibromyoma of Uterus with Leiomyosarcomatous Degeneration with Secondary Invasion of the Transverse Colon.—Dr. C. H. KAYE.

(1 and 2) Spontaneous Rupture of the Uterus.—Dr. A. T. MCNEIL.

Hydrops Fætalis in One of Rh-positive Twins.—Dr. I. M. TUCK and Dr. K. A. K. HUDSON.

Hydatidiform Mole in Repeated Pregnancies and Invasion of Uterus by Tumour of Doubtful Origin. For Diagnosis.—Mr. EWART WILLIAMS.

¹Subsequent histological examination has shown an area of pituitary necrosis.

Section of Odontology

President—HUMPHREY HUMPHREYS, O.B.E., M.C., M.B., F.D.S.

[April 26, 1948]

Experimental Investigation Into Factors Concerning the Growth of Cysts of the Jaws

By P. A. TOLLER, L.D.S.

INTRACYSTIC PRESSURE

THERE is much evidence to suggest that certain cysts increase in size by reason of the fluid tension within them. This was recognized early by the French and German surgeons after the discovery that opening a cyst into the mouth checked further growth and subsequently led to a decrease in size of the tumour. Cysts occurring between the roots of teeth cause these roots to be displaced apart as if by pressure (cases quoted by Potts, 1927). Another observation concerns the migration of teeth associated with dentigerous cysts. Included teeth are frequently found lying at relatively great distances from their sites of development. These occurrences are strongly suggestive of a pressure effect, since if the growth of the cyst had simply been due to the proliferation of tumour cells then it would be expected that the tooth would remain static in relation to the bone and the tumour would grow around and pass it.

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In a study of intracranial pressure O'Connell (1943) demonstrated an experiment to show that variations in pressure were imperfectly transmitted through a system which incorporated a ventricular cannula of 2 mm. internal diameter when the rate of variation was about that of the cardiac rhythm. When a lumbar-puncture needle of small bore was used (0.8 mm. bore) the inaccuracy was very pronounced, though slow variations (four variations per minute) can be recorded accurately through a system of such narrow bore. This consideration is only of importance when measuring variations of intracystic pressure with the cardiac pulse.

Manometer.—A simple direct manometer was not considered sufficiently accurate to measure intracystic pressure, owing to the fact that fluid must flow out from the cyst cavity in order to cause the manometer to register. This egress of fluid slightly reduced the volume of the fluid in the cavity and consequently the pressure within the cavity diminishes, so the final reading is not strictly true. This error is most important when examining small cysts completely surrounded by bone.

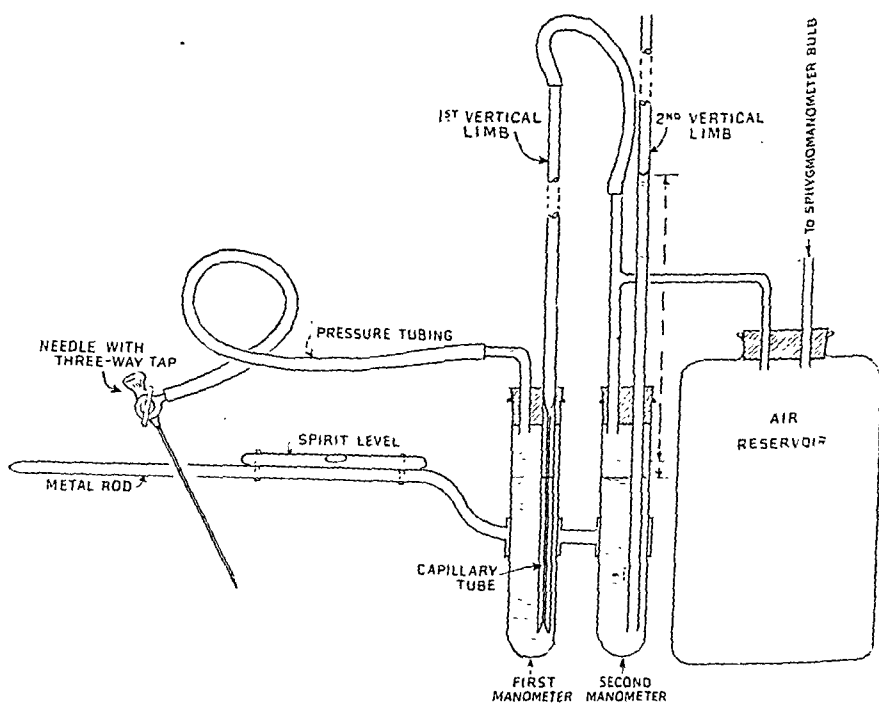


FIG. 1.—Manometer for measuring intracystic pressure.

A method was evolved in which the final reading was of that pressure required to prevent egress of fluid from the cyst. This method of applying counter-pressure effectively overcomes the tendency to inaccurate recording which might be due to blockage of the cannula by the semi-solid nature of the cyst fluid.

Description of apparatus.—A Greenfield's pattern spinal cannula is connected by 12 in. of narrow pressure tubing to the reservoir of the first manometer. The vertical limb of this manometer is made so that it is of very narrow bore in its lower part. This capillary portion is provided with a fixed mark. The level of this mark is made to correspond exactly to the vertical height of the tip of a horizontal rod which is fixed rigidly to the manometer. A spirit level is fixed to this rod. (Error would be introduced if there was a difference in vertical height between the manometer and the cyst cavity, owing to a siphon effect (fig. 1).)

The upper end of the vertical limb is connected by rubber tubing to an enclosed space above the reservoir of a second manometer. This space is also connected to a sphygmomanometer bulb, an air reservoir of at least 500 c.c. being included in the system in order that even pressure variations can be exerted by the rubber bulb.

Operation.—A sterile technique is adopted when using the apparatus, the cannula and pressure tubing being boiled and filled with sterile water.

The apparatus is held next to the patient at the level of the cyst, reference being made to the spirit level provided on the horizontal arm.

The cannula is first introduced into the cyst cavity with its tap in the closed position, and held to cause as little tension on the surrounding tissues as possible. The tap is then turned to connect the cyst cavity with the first manometer. Intracystic pressure will cause water to rise in the limb of the manometer. Air pressure is then applied to the surface of the water in this limb until the water is returned to, and maintained at, its original level. The air pressure needed to prevent egress of fluid from the cyst cavity is then noted by recording the water levels in the second manometer.

This reading represents the hydrostatic pressure within the cyst. Correction can be made for the volume of the portion of cannula which is inserted within the cyst cavity.

SUMMARY OF INTRACYSTIC PRESSURES FOUND IN A SERIES

Dental cysts

Highest recorded pressure	95.0 cm. water
Lowest recorded pressure	56.6 cm. water
Average pressure in 51 cases (to nearest whole number)	70 cm. water

Dentigerous cysts

Highest recorded pressure	94.7 cm. water
Lowest recorded pressure	22.5 cm. water
Average pressure in 9 cases (to nearest whole number)	65 cm. water

Adamantinoma

3 cases (1)	10.0 cm. water
(2)	12.0 cm. water
(3)	8.5 cm. water

Developmental cyst—premaxilla

One case—Recorded pressure	—87.5 cm. water
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This series of cases is too small to draw any significant conclusions, but the following points were noted:

- (1) The intracystic pressures fall within similar limits, whether the cyst, either dental or dentigerous, was large or small, or whether the patient was young or old.
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- (3) The pressures in the three adamantinomata were much lower than those found in other types of cyst.

Variation of Cyst Pressure with Cardiac Pulse

It was noticed in several cases that the water level in the first manometer varied slightly with the cardiac pulse. Using a cannula and capillary tube of much larger diameter than usual in order to reduce the fluid inertia of the system, an attempt was made to assess the intracystic pressure differences due to the cardiac pulse.

Fluctuations in the first manometer limb were observed and readings were taken of the counter-pressure required to return the fluid level: (1) To the original level at maximum displacement of the fluid column; (2) to the level at minimum displacement.

In the three cases tested, the average pressure difference between the displacement levels was 4.5 cm. water. This figure will be inaccurate, erring on the low side of the true figure, owing to the inherently high fluid inertia of the system when recording such relatively rapid changes of pressure.

DISCUSSION

The foregoing experiments serve to confirm that positive fluid pressure exists within cystic cavities. The pressures recorded are all above capillary blood-pressure which Hill gives as about 3.5 cm. of water. (Starling states that capillary pressure can often be as high as 10 cm. water.)

It is obvious that if this full intracystic pressure was exerted upon the surrounding capillary bed, the walls of the capillaries would collapse resulting in cessation of the local circulation of blood. There may in fact be a slight compression of the surrounding capillaries, producing a slight ischaemia. This may be a factor in the pressure atrophy of the surrounding bone.

In some cysts it is possible to find degenerating cells close to a capillary. Such cases are not easy to explain on the grounds that the degeneration is caused by the cells being too far removed from a blood supply unless that blood supply itself is inadequate. Local ischaemia due to abnormal pressure of the cyst may hasten the degeneration of the cells of a cyst lining.

It is likely, however, that the main bulk of the cystic pressure is borne by its own epithelial and fibrous walls, in a similar manner to the way in which blood-vessels carry a positive pressure.

In a study of intracranial pressure O'Connell (1943) demonstrated an experiment to show that variations in pressure were imperfectly transmitted through a system which incorporated a ventricular cannula of 2 mm. internal diameter when the rate of variation was about that of the cardiac rhythm. When a lumbar-puncture needle of small bore was used (0.8 mm. bore) the inaccuracy was very pronounced, though slow variations (four variations per minute) can be recorded accurately through a system of such narrow bore. This consideration is only of importance when measuring variations of intracystic pressure with the cardiac pulse.

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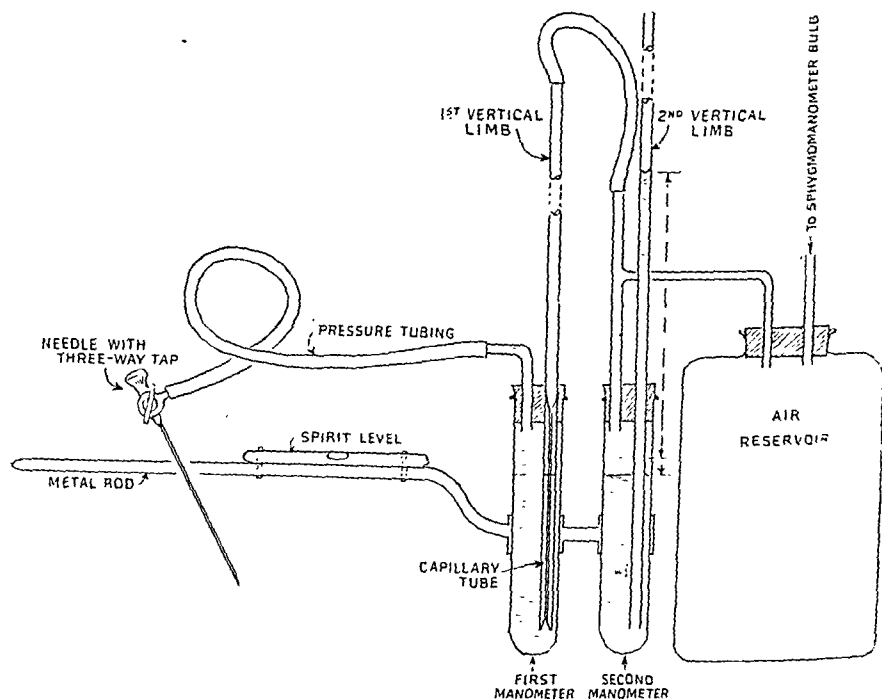


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The upper end of the vertical limb is connected by rubber tubing to an enclosed space above the reservoir of a second manometer. This space is also connected to a sphygmomanometer bulb, an air reservoir of at least 500 c.c. being included in the system in order that even pressure variations can be exerted by the rubber bulb.

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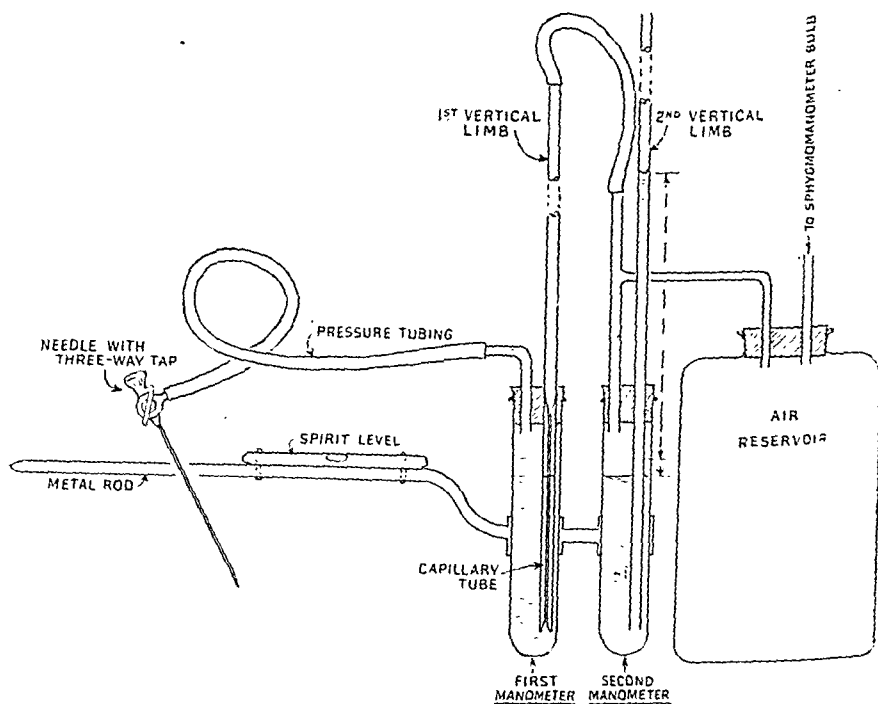


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Operation.—A sterile technique is adopted when using the apparatus, the cannula and pressure tubing being boiled and filled with sterile water.

The apparatus is held next to the patient at the level of the cyst, reference being made to the spirit level provided on the horizontal arm.

Description of osmometer.—Two brass cylinders are provided with flanges which are ground together to have a perfectly flush fit. The cylinders are held on a hinged clamp so that they may be swung apart or brought tightly together. The chamber in each cylinder is slightly sloping upward away from the face of the flange and is accurately machined to be of equal volume with the other chamber. At the base of each cylinder is a narrow inlet tube leading to a small tap provided with an attachment for a record syringe (figs. 2 and 3).

A vertical glass capillary tube leads out from the uppermost point in each chamber and a horizontal mark is provided at the same level in each tube. The design is such that liquids introduced through the inlets at the base of each chamber fill the chamber and rise into the capillary tubes without the inclusion of air bubbles. The inlet tubes are also directed so that the incoming fluid tends to flush over the face of the flanges, so bringing it into immediate intimate contact with any membrane that is placed over the face of the flange.

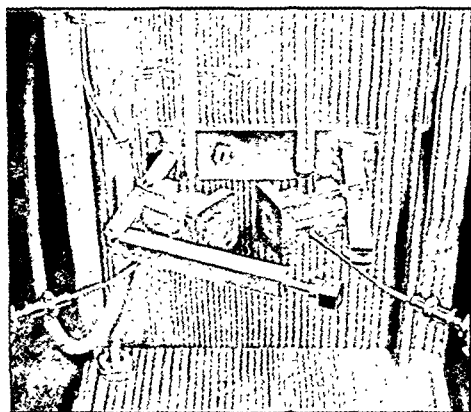
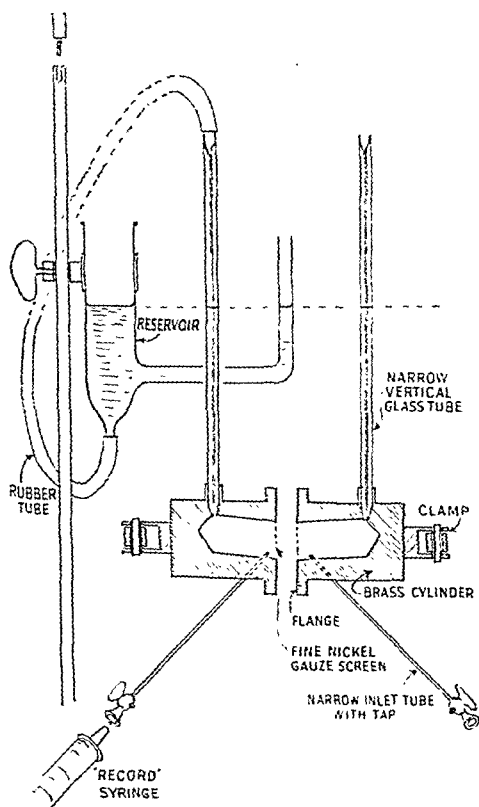


FIG. 3.—Osmometer with cylinders apart ready for reception of semipermeable membrane.

FIG. 2.—Diagram of osmometer used in the experiments.

A fine nickel gauze screen is let into the mouth of each chamber. This ensures that any membrane clamped between the cylinders will be supported firmly and atraumatically and it will prevent bulging or bursting of the membrane if an excessive pressure is applied to one side of it.

An extra manometer reservoir, provided at the side of the apparatus, is connected to the top of one of the vertical capillary tubes by rubber tubing. By raising or lowering this reservoir (usually filled with oil of known specific gravity) a counter-pressure can be applied to the surface of the fluid in the capillary tube. The reservoir can be moved up or down a vertical rod, this rod being supplied with an extension piece to enable the reservoir to be held at a greater height if necessary.

Operation of apparatus.—A membrane of unknown permeable qualities may be clamped between the two cylinders, and fluids of known character introduced simultaneously into the chambers on either side of it by injection with Record syringes. The two liquids are levelled to the marks on the capillary tubes and the taps closed.

The system then consists of two equal volumes of fluids separated by the membrane under examination.

Those studying pathology in relation to the orthodontic traction state that the pressures used in orthodontic appliances must not cause a tooth to apply a pressure on its surrounding structures more than capillary pressure, otherwise necrosis of bone may result instead of physiological absorption. Necrosis of bone is not observed in relation to cyst growth. It would seem that the actual expansive pressure that the cyst exerts on the surrounding tissues is likely to be very small, i.e. below 3.5 cm. water.

Intracystic pressures which have been recorded can be considered as high in comparison with capillary blood-pressure; they are comparable to pressures found in arterioles. The only arteries of any large size that are found in relation to cysts of the jaws are the inferior dental vessels and sometimes a fairly large vessel is encountered on the deep posterior aspect of maxillary cysts.

No opportunity has yet presented itself for the study of pressure in enclosed hamatomata. No "bone cysts" have been investigated, although this type of fluid collection will be studied if the opportunity arises, since it may lead to a better knowledge of the pressures that may be expected in passive fluid collections in the tissues. Such study would provide a clearer idea of the part played by simple hydrostatic effects (i.e. the pressures due to blood-pressure, muscle-tone, posture) or cyst pressure.

The positive pressure remains much the same whether the cyst is small or large, in fact this pressure is maintained even when the cyst wall is just beneath the surface of the oral or nasal mucous membrane. An investigation was therefore carried out to determine whether there were other than purely hydrostatic factors maintaining the positive pressure.

THE OSMOTIC FACTOR

It has seemed most likely that the factor causing the pressure within a cyst to be raised above the pressure of the surrounding tissues would be a difference in osmotic tension. This was suggested by James (1926) and has been mentioned from time to time since he published his experiments in connexion with cysts. Thoma mentions that it is possible that osmosis maintains intracystic pressure, and in 1939 Tratman wrote a paper suggesting that diffusion of fluids influenced cyst growth. In fact, he appears to have performed the only experimental work in the dental field to verify this theory. His experiments consisted of aspirating the contents of four cysts and observing that at the end of twenty-four hours the cyst cavities had again become distended with fluid. This interesting observation, which he recorded with care, suggests that the refilling of the cysts occurred by osmosis. However, any fluid remaining in the cavity after the original aspiration would need to have a fairly high osmotic tension, above that of the surrounding tissues, otherwise the incoming fluid from the tissues would bring about an osmotic balance before the cavity had completely refilled. It may therefore be a simple transudation of fluid from the surrounding tissues.

In other fields it is well to note that Schalyt (1930) suggested that the development of ovarian cysts was dependent on secretory activity and disturbance in osmotic equilibrium of the ovarian tissues. Gardner (1932) showed that the contents of old subdural cysts were of higher osmotic tensions than the surrounding cerebrospinal fluid and he suggested that the increase in size of these cysts was due to osmosis.

Osmotic pressure of a solution depends upon the number of submicroscopic particles in solution or colloid suspension. Animal tissues are pervious to water and dissolved crystalloids but are impervious to colloids except under certain circumstances. It will be seen that if a large molecule should break down into two simpler molecules, the number of particles dispersed in solution will be increased and the osmotic tension will rise, independent of the chemical nature of the molecule. If substances such as cytoplasm, nucleoprotein and other complexes associated with vital cells should be broken down to simpler molecules, as would be expected in a degenerative process in the tissues, then the osmotic tension of the resulting product would rise. If the products were surrounded by a membrane permeable to the solvent and impermeable to the solute then the pressure within that membrane would rise. This phenomenon may account, at least in part, for the presence and maintenance of positive intracystic pressure.

With this in view, an investigation was proposed: (a) To examine the epithelial linings of cysts and to determine whether they act as semipermeable membranes; (b) to examine some chemical and physical properties of cyst fluid.

Experimental

An apparatus has been devised to examine the permeability of freshly dissected cyst membrane.

The apparatus was also designed to study the osmotic tension of cyst fluid, blood and tissue fluids, and to compare the osmotic tensions of fluids directly through actual cyst membranes and through artificially prepared membranes.

cyst. This will exert a pressure dependent upon the hydrostatic pressure within the surrounding vessels and its effect may be likened to that of a sphygmomanometer cuff. Then there is the effect of "tissue pressure" mentioned by Starling, which is the result of the tone of the living tissues and amounts to only a few millimetres of water. There is also the effect of the osmotic differences between cyst fluid and blood and the intervening tissue fluid which is in common relationship to both.

It has been shown that the osmotic pressure of cyst fluid varies over relatively small limits, which variations would be insufficient to account for the wide variations of pressure actually found within cysts. It has also been demonstrated that variations in fluid pressure due to the cardiac pulse (approximately 5 cm. water) are greater than the difference in osmotic pressure between blood and cyst fluid, so that it would seem that the main factor influencing positive intracystic pressure is the hydrostatic factor due to the surrounding vascular network.

If, for instance, a small semipermeable sac is partly filled with a hypertonic solution and it is immersed a few inches beneath the surface of some water, then, so long as the sac is not completely filled by its contained fluid, the hydrostatic pressure within the sac will be the same as that of the surrounding water. Only when the sac becomes filled with fluid and the walls become taut does the pressure within the sac rise above that of the surrounding water. Then the pressure within it is the sum of the difference in osmotic pressure between the fluid and water, and the pressure due to the depth it is immersed in that water.

Hydrostatic pressure in the larger capillaries and arterioles varies between 10 cm. and 100 cm. of water (Starling).

If hydrostatic equilibrium is attained between the cyst and the surrounding vascular and tissue pressure, there is always the tendency to slightly greater pressure within the cyst due to the osmotic imbalance and it is likely that this slight but ever-present osmotic pressure is responsible for the increase in size of the cyst.

If the osmotic imbalance is always present in the cyst fluid, despite the fact that the cyst grows larger and that there is always a tendency to bring about isotonicity, then it follows that there must be a continual supply of substances maintaining the hypertonicity.

It has been previously mentioned that degeneration of tissues is likely to produce a liberation of substances of lower molecular weight than those which make up vital tissue. Analysis of the proteins involved in vital tissue is itself a vast study, and one about which knowledge is yet in its infancy. Suffice it to say that molecular weights as high as 300,000 have been calculated for certain tissue proteins. An analysis of cyst fluid shows that it is made up largely of simple proteins with molecular weights of about 30,000. Thus it is likely that the breakdown of complex tissue proteins into a larger number of molecules of simple proteins is responsible for the raised colloid osmotic pressure found in cyst fluid.

I wish to express my special thanks to Mr. Rainsford Mowlem, Mr. B. W. Fickling and Dr. A. B. MacGregor at the Plastic and Jaw Unit, Hill End Hospital, for their patience and assistance.

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The behaviour of the membrane can be assessed by observation of the fluid levels in the capillary tubes. A rise of level in one tube would be accompanied by a depression in the other if an osmotic transference takes place through the membrane.

The difference of osmotic tension between the two fluids, if the membrane is known semipermeable membrane, can be measured by applying a counter-pressure so that the levels in the two capillary tubes are kept the same so that equal volumes and the original concentrations of solutions are maintained. An oil manometer is used, oil not being miscible with the fluids under investigation, and, being of a small specific gravity, oil gives a good range of measurement for small differences in osmotic pressure.

First experiment.—Experiments were performed using freshly dissected cyst wall from 12 cases of dental cysts and 6 cases of dentigerous cysts. The wall was placed between the manometer cylinders and Ringer's solution introduced on one side. Ringer's solution to which had been added 5% egg albumin was introduced on the other side.

In all cases fluid passed through the membrane to the side containing the dissolved albumin. Transference of fluid continued until the capillary tube overflowed on one side and the fluid level disappeared in the other tube.

Second experiment.—A group of tests was made using direct comparisons of whole blood and cyst fluid taken simultaneously from the same patient. A known semipermeable membrane of cellophane was used.

In 11 cases of uninfected dental and dentigerous cysts: 4 cases showed no registrable osmotic difference, 7 cases showed cyst fluid to be of slightly higher colloid osmotic pressure than whole blood.

In these last 7 cases an average osmotic pressure difference of 3.7 cm. of oil (sp. gr. 0.8) was recorded, which represents an average pressure difference of 2.96 cm. of water.

Third experiment.—In 5 cases, the freshly dissected cyst membrane was placed in the osmometer and the aspirated cyst fluid from the same patient introduced on the epithelial side of it while the patient's blood was introduced on the other side.

In one case only (from a small dental cyst) was there a rise on the side of the cyst fluid (0.8 cm). The other 4 cases showed no change in level.

Summary of Experiments

- A. I. A manometer has been described for accurate measurement of hydrostatic pressure within closed fluid-filled cavities within the body.
- II. Intracystic fluid pressures have been measured in a series of cases of uninfected cysts before surgical interference.
- III. Pressures ranging between 8.5 cm. of water and 95.0 cm. of water have been recorded.
- IV. Lower pressures were noted in adamantinoma.
- V. Blood-pressure has a direct effect on intracystic pressure.
- B. I. An osmometer suitable for examination of the permeability of cyst wall and for comparing osmotic pressures of cyst fluid and blood has been described.
- II. It has been shown that freshly dissected cyst wall behaves as a membrane impermeable to a colloid (albumin) and permeable to crystalloids and water.
- III. Osmotic tensions of cyst fluid and blood from the same patient have been measured and compared directly. In some cases the osmotic tension of cyst fluid was found to be greater than that of the blood. In other cases no measurable difference in tension was noted. In no case has the cyst fluid shown a lower osmotic tension than that of blood.

DISCUSSION

The results of the foregoing experiments support the theory that positive hydrostatic pressure within cysts is a factor influencing their growth. The fact that the exteriorization of a cyst cavity effectively checks further growth is strong clinical evidence in favour of the theory, although this does not rule out the possibility of the effect of accumulated products of degeneration of the tissues stimulating epithelial cells to proliferate.

The experiments indicate that the cause and maintenance of positive cyst pressure in dental and dentigerous cysts are likely to be related to the osmotic tension of the cyst fluid.

The positive pressure within a cyst is liable to be the result of several forces. First, there is the effect of pressure of the surrounding vascular network within the walls of the



FIG. 1.

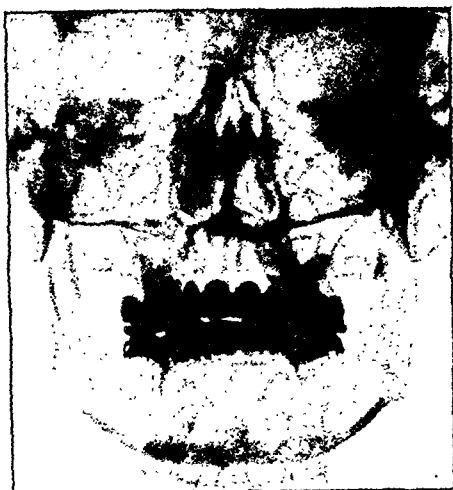


FIG. 2.



FIG. 3.

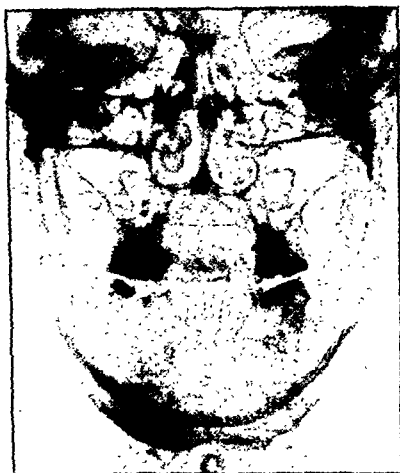


FIG. 4.

Figs. 1 and 2 (February 1946) show the immediate post-operative condition. The oblique lateral view shows clearly the anteroposterior lines of sectioning of the rami and the degree of displacement necessary to reduce the prognathic mandible for the teeth to be put into normal occlusion. Figs. 3 and 4 (February 1948) show the same views. Comparison shows not only the completeness of osseous repair, but also the plastic moulding by which the sharply projecting corners at the sites of section have been rounded off.

I am greatly indebted to Drs. W. H. Coldwell and F. A. Allchin for the skiagrams of this case.

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Kostecka's Osteotomy for the Correction of the Prognathous Mandible¹

By C. BOWDLER HENRY, L.D.S.Eng., M.R.C.S., L.R.C.P.

I SHOWED this patient (M. K.) before the Odontological Section in April 1946, nine weeks after operation, as an example of Kostecka's closed method of bilateral osteotomy of the rami for the correction of mandibular prognathism. I had followed Kostecka's technique precisely as to the surgery, but I had varied the form of fixation. Kostecka favours fixing the floating mandible by ligating the upper and lower teeth together with orthodontic wires applied after cutting through the rami. The operation is thus extended by a somewhat fiddling procedure which would also have manifold disadvantages in cases where several teeth were missing. It seemed to me, when considering this operation, that the duration of operation could be markedly reduced and a more positive result, according to pre-operative planning, would be obtained if cast metal splints with a simple rapid interlocking device were to be cemented on to the upper and lower teeth previous to operation. I modified Kostecka's technique accordingly.

This patient, therefore, when shown originally before the Section, was still splinted and the sites of puncture for the needle and saw were clearly visible. Immobility was maintained for six weeks after which progressive function was allowed and within the next fortnight he was masticating ordinary food. The splints were left in situ so as to discipline the mandible for a further period of ten weeks. After they were removed the final occlusion was established by slight grinding of the cusps. Mastication became normal and there was no limitation of opening.

In view of the novelty of the operation and certain adverse criticism when the case was shown, I offered to keep the Section informed as to progress. Accordingly, the patient was demonstrated again twelve months later (Clinical Meeting, Odontological Section, April 1947) as a clinically completed case, when the functional and æsthetic results were seen to be entirely satisfactory. This demonstration of the final skiagrams on April 26, 1948, concludes the case.

¹The follow-up and final skiagrams of a case previously shown before the Odontological Section, 1946, *Proc. R. Soc. Med.*, 39, 646.

Section of Radiology

President—J. S. FULTON, C.B.E., M.D.

[May 21, 1948]

Report from the Mozelle Sassoon Department, St. Bartholomew's Hospital, London, E.C.1

The Million-Volt X-Ray Plant — Its Development and Application

By G. S. INNES, B.Sc., A.M.I.E.E., A.Inst.P.

THIS note, which gives a short history of the million-volt X-ray equipment at St. Bartholomew's Hospital, and some of the physical advantages we believe million-volt X-rays have over those generated at 200-250 kilovolts, is only intended to indicate the general background conditions under which the clinical results reported in the two following papers were obtained.

History of the plant.—It was in the year 1934 that the Cancer Committee of St. Bartholomew's Hospital, with the generous financial backing of Mrs. Meyer Sassoon, contracted with Messrs. Metropolitan Vickers Electrical Company for the supply and installation of a continuously evacuated X-ray tube, together with the necessary High Voltage D.C. Generators, to operate at a guaranteed voltage of 600,000 volts, with the proviso that an attempt would be made to operate continuously at one million volts. At that time, the High Voltage and Vacuum Sections of Metropolitan Vickers Research Department, under the direction of Dr. Allibone and Mr. Bancroft [1, 2], had designed, built, installed and had operated for some eighteen months, two 200,000 volt continuously evacuated X-ray tubes at Sheffield Royal Infirmary. These were the first demountable tubes to be used for radiotherapy in this country, and the accomplishment was in no small part due to the encouragement and enthusiasm shown by Dr. Ellis, then Director of the Therapy Department at Sheffield.

Tube.—From 200 kV to 1,000 kV was a considerable step, involving many unknown factors. In the short time available for experimentation, an attempt was made to

find how far the behaviour of supervoltage tubes could be predicted from theoretical calculations [3]. From these researches grew the design of the equipment as it was installed in St. Bartholomew's Hospital in the second half of 1936 [3, 4 and 5] (fig. 1). The exploded view of the equipment shows that the tube spans the treatment room, projecting on the left into the room which houses the 500 kV Positive D.C. Generator and on the right into the Negative Generator room.

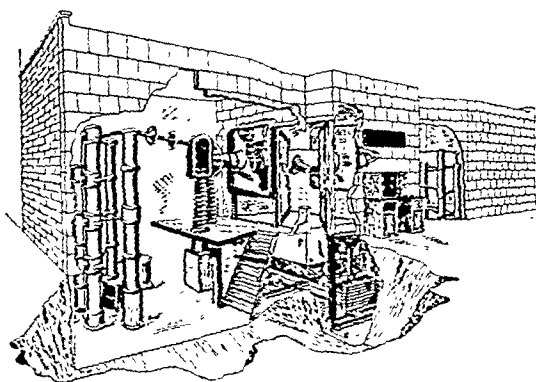


FIG. 1.—Perspective view of 1,000 kV X-ray tube installation.

The vacuum envelope of the tube proper comprises a 14 in. diameter steel cylinder

An Appliance for Exerting Pressure Upon a Skin Graft of the Lip or Cheek

By J. F. LOCKWOOD, M.R.C.S., L.R.C.P., L.D.S.Eng.

THE application of a pressure dressing to a skin graft of the lip or cheek is made difficult by the mobility of the part, and, in cases where teeth have been lost, by the absence of anything against which pressure may be exerted.

The use of a suitable acrylic appliance in such cases facilitates immobilization of the part and the maintenance of firm and consistent pressure upon the graft.

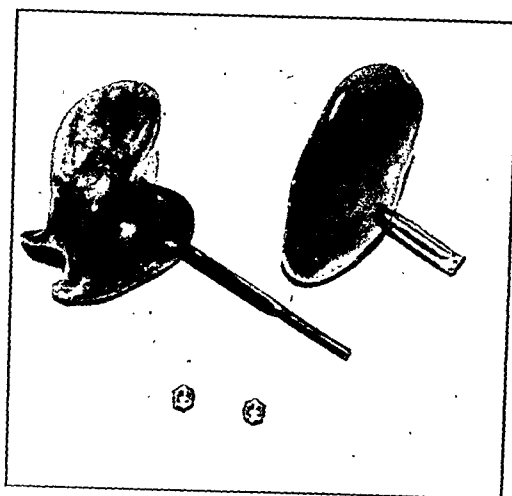


FIG. 1.



FIG. 2.

Such an appliance consists of two pieces: an intra-oral part made to fit the area normally covered by any necessary denture—upper or lower, as may be convenient—and having a smooth labial or buccal face fitting the inner aspect of the lip or cheek; and an external part in the form of a cupped plate made to overlie the area to be grafted. The two pieces are articulated by means of square rod and tubing, the former being threaded to take a lock nut (fig. 1).

At operation the graft is inserted, the intra-oral part of the appliance fitted, the graft covered with a flavine and paraffin pack, and the external part of the appliance screwed home (fig. 2).

The appliance illustrated was worn with moderate comfort and without adjustment for twenty-two days. On its removal the graft proved to be in excellent condition.

the section of the treatment room floor under the tube. These two movements, rotation of the applicator cylinder and movement of the floor, provide positioning movements which in practice are found to be as simple and satisfactory as those of the normal 200 kV unit.

Generators and control.—The two high-voltage D.C. generators, employing the Cockroft voltage multiplier circuit, are fitted with four 250 kV continuously evacuated rectifiers each. The generators on test generated a total voltage of 1.5 million volts and produced a thirty-foot-long spark in air. The kilovoltage, applied to the tube from these generators, is in the hospital indicated on the control desk by means of direct reading resistance voltmeters. The result is simple and accurate control conditions—tube kilovoltage and X-ray monitor output and/or dose given.

Protection.—The treatment room and generator rooms are surrounded by barytes brick walls, which provide such a degree of protection outside these rooms that X-ray films can with safety be kept in the department for many years. In the treatment room with the shutter closed, the protection is such that with the tube operating at one million volts and 5 kilowatts, the leakage intensity anywhere in the treatment room is not greater than one-half of tolerance.

Operation.—The tube, as installed in 1936, was composed of the following electrodes: (a) The steel vacuum envelope which was earthed; (b) a six-element filament assembly which was supported by a steel cathode support tube bolted to the end of the tube negative porcelain and connected to the H.V. output terminal of the negative generator; and (c) a gold disc target supported by a steel target support tube, bolted to the tube positive porcelain and connected to the positive generator output terminal.

One hour after the final erection and evacuation of the untried tube at the hospital, a voltage of 700 kV with a load current of 3 ma. was attained with perfect stability. On attempting to raise the voltage applied to the negative end of the tube above 350 kV, the electrical stresses on the steel cathode support tube became so great that the support tube acted as an electron emitter and many milliamperes of electrons flowed from it to the tube envelope. The calculated electrical gradients at this voltage were much below those at which this phenomenon was expected. This was one of the unknown factors, the possibility of which had been envisaged. The low voltage onset of field currents was caused by incalculable high gradients due to microscopic roughness of the electrodes, vitiating simple theory. Thereon, it was decided that the equipment would be used for treatments at 700 kV, while modifications to the tube were carried out during the week-ends. This was rather a harassing process since the equipment had to be in operation first thing on Monday mornings at 700 kV without fail.

After many modifications the tube, as it is now (fig. 2A), was put into operation, in 1939, on patients at one million volts 4 to 5 ma. It will be seen that the tube has become a multiple acceleration tube, in which the electrons are accelerated from the cathode (k) through three nozzles in four stages of 250 kV to the target (f), i.e. from 500 kV negative to 500 kV positive. The radial tube gradients are catered for by the intermediate thin steel tube electrodes (l, n) connected to the mid-potential points on each generator.

Reliability and maintenance.—The vacuum pumping plants on the tube and rectifiers have operated day and night continuously since the plant was installed, some 95,000 hours, equivalent on the electric motors to about three million car miles. The oil in the diffusion and rotary vacuum pumps has not been changed since 1937 and, except for some distillation of oil from the first diffusion pump, necessitating, after seven years, extraction of excess oil from the O₂s, failures of the pumping plants have been rare and primarily caused by brushes sticking in the rotary pump driving motors.

The longest single period of breakdown, since the plant has been operating at a million volts, has been one afternoon. Occasionally there has been a stoppage of one and a half hours while a rectifier filament is replaced. These rectifier filaments have been replaced normally about every 1,250 hours, while the rectifier stacks have been dismantled, cleaned, and the electrodes burnished

with bolted-on insulator on either end; the whole being evacuated by two 250 litre per second pumping plants. Round the portion of the tube envelope, spanning the treatment room, is a hollow steel cylinder filled with some eight tons of lead shot. This cylinder has one portal in it, and the cylinder being rotatable, it acts both as the protection and the X-ray shutter. In the "safe" or shutter shut position the portal points upwards into the lead block suspended above the centre of the tube (fig. 2A).

Surrounding the "lead" cylinder is the outer or "applicator" cylinder which carries the beam sweep lead protection, the control ionization chamber, the filters

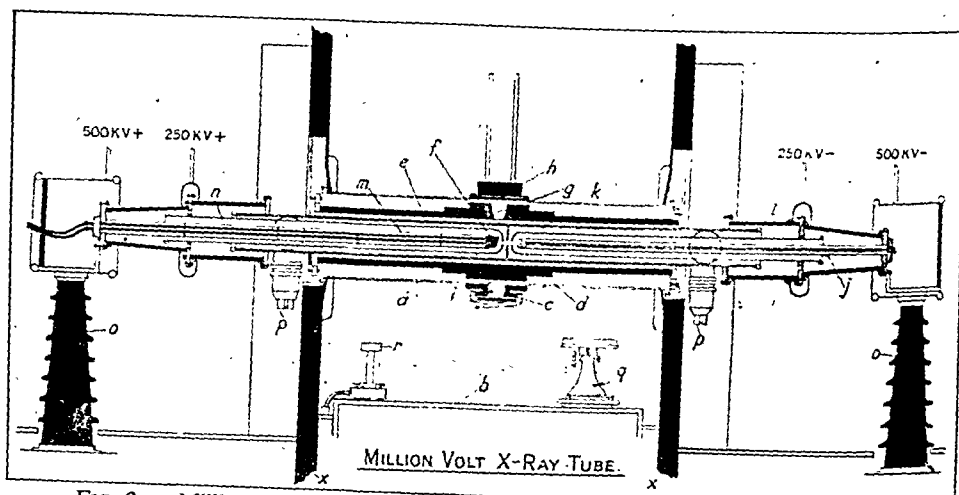


FIG. 2A.—Million-volt X-ray tube. (Reproduced from *Brit. med. Bull.*, 1946, 4, 52.)

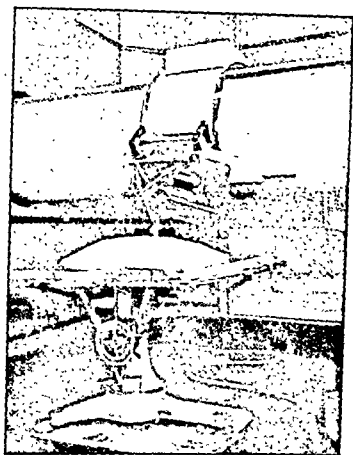


FIG. 2B.—Light-centring device. (Reproduced from "Supervoltage X-ray Therapy", by R. Phillips, London.)

and the beam limiting devices. The control ionization chamber is cable connected to an indicating instrument on the control desk, which gives both monitor dosage rate and monitor dose given. The "applicator" cylinder is rotatable, such that the angle of the X-ray beam emerging from the applicators can be varied from pointing vertically downwards, forward and upwards to 24° above horizontal (i.e. 114° rotation in all). Since the tube is some 30 feet long, overall, and weighs about 10 tons, adjustment of the patient to the tube is more easily accomplished by raising or lowering

The output from the tube operating at a million volts and 4.5 ma. is equivalent to that which would be obtained from 7 kilograms of radium under the same conditions and the beam wavelength is approaching that of gamma rays.

PHYSICAL ADVANTAGES

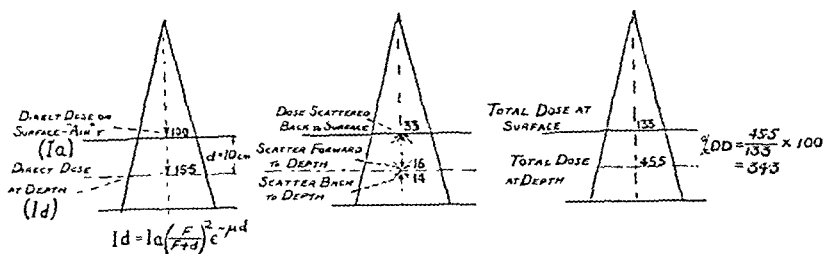
Depth dose.—The main physical advantage in operating with million-volt X-rays, when compared with the usual 250,000 volts X-rays, is the gain in depth dose; that is the dose at a depth relative to the dose at the surface. For comparison, consider the usual therapeutic conditions and our own, for a beam of 10×10 cm. and at 10 cm. depth.

The usual conditions are 250 kV, 1.5 mm. Cu H.V.L., 50 cm. F.S.D.

Our conditions are 1,000 kV, 9.3 mm. Cu H.V.L., 100 cm. F.S.D.

If we give an air dose of 100 r under each condition (fig. 3), the total dose at 10 cm.

10x10cm 50cm FSD FIELD 250kV 1.5mm Cu HVL



10x10cm 100cm FSD FIELD 1000kV 9.3mm Cu HVL

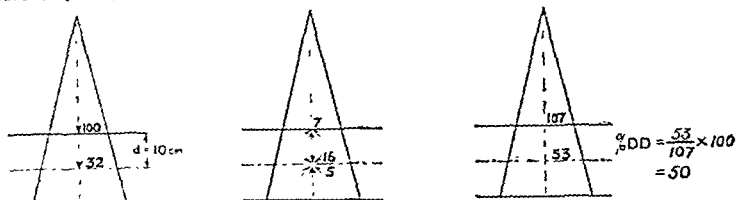


FIG. 3.—Composition of dose at depth, at 250 and 1,000 kV.

deep at 250 kV is 45.5 r and at a million 53 r, a gain with a million, but not a great one. However, the shorter the wavelength of the X-rays used, that is the higher the kilovoltage employed, the more forward becomes the scatter from the absorption processes. Therefore at 250 kV, there is considerably more scatter back to the surface than there is at a million. The result is that the surface doses are 133 r and 107 r respectively. This gives percentage depth doses, that is the doses at the depth as a percentage of the surface doses as 34.3 and 50% respectively, representing a gain of about 50% in the dose at the depth by employing million-volt X-rays.

Now consider how this happens apart from the effect of the large difference in surface backscatter. The dose at a depth can be regarded as being made up of three components (fig. 3); first, the direct or through dose, comprising the primary rays which penetrate right through the patient to the depth and are absorbed there; secondly, forward scattered rays, scattered from the part of the patient above the level of measurement; and thirdly, backscattered rays, scattered back from the part of the patient below the level of measurement.

At 250 kV the direct component at 10 cm. depth is only 15.5 r while at a million it is 32 r. This great difference is due to the higher penetration of the million volt rays. Not only this, but the direct component is nearly $\frac{2}{3}$ of the total dose at the depth at a million volts, whereas at 250 kV it is only approximately $\frac{1}{3}$. Therefore if the direct component

every 2,500 hours. Since the final modification to the tube in 1939, the tube has operated approximately 15,000 hours at a million volts and until the middle of 1947 it had not been dismantled. Then it was dismantled, primarily to alter one of the electrodes, so that a new type of target could be accommodated, and secondly for inspection, since a slight instability had appeared, which occasioned some inconvenience during the initial application of voltage every Monday morning. The only deterioration found was flaking of the surface of the nose of one of the intermediate electrodes, due to an occlusion of sand in the steel of the electrode. Tube filaments, of which there are six, now generally last for 1,000 hours each. The gold-faced target, on an average, has been replaced every 3,000–4,000 hours, not because it has been leaking, but because by that time the gold surface has become extremely rough.

At the commencement of the war, the department was closed for three months, but during the rest of the war, although the department lost its ceilings, windows and doors three times, and part of its roof another time, the plant functioned, providing that electrical and water supplies were available; sensitive relays and mechanisms damaged by concussion and vibration being temporarily locked in, by match sticks, until patients' treatments were completed for the day, whereon repairs were carried out. During the nine years of operation at a million volts, the expenditure on maintenance material, and replacements used on the plant has been under £200.

Clinical intention.—The intention of the clinical investigation was to find whether there was an improvement in the relative lethal effectiveness of X-rays on malignant cells when compared with normal cells as the wavelength of the radiations was reduced, other factors being kept the same. It soon became obvious, during the initial period of operation at 700 kV, that this simple test was impossible of accomplishment, since there were so many complicating ancillary factors, which automatically appeared with change in wavelength; for example, change in depth dose altering the dose distribution in the normal tissue surrounding the malignant cells, and changing to some unknown extent the indirect action on the tumour. Therefore it was decided to use the tube under its best conditions, with all the benefits it gave from the physical aspect, and from the clinical results to try to assess the overall change in lesion response and whether it could be attributed directly to change in wavelength.

X-ray beam limitation.—From our early experience with applicators at 700 kV, 60 cm. F.S.D., it was apparent that at a million volts and one metre F.S.D., applicators would be too heavy to handle. An adjustable diaphragm was constructed (fig. 2B), fitted with a light beam device which indicates the X-ray field size, shape and position. This diaphragm makes available any field size from 4×5 cm. to 40×40 cm., in centimetre steps, some 450 different field sizes and provides no limitation as far as field planning is concerned. The one disadvantage of this diaphragm is that, owing to its size, it is located at 45 cm. F.S.D., and with the existing focal spot size of 2.5 cm. diameter, a considerable "inumbra" and penumbra is cast on the fields at 100 cm., the normal operating F.S.D. It is hoped that when manufacturing facilities are available it will be possible, by reducing the focal spot and by adding secondary diaphragms, to remove these disadvantages.

Treatment Conditions—

1937–39: 700 kV, 5 ma., 60 cm. F.S.D., filter 3.2 mm. Fe, 1.5 mm. Al, 2 mm. Pb, 2.4 mm. Sn, 0.5 mm. Cu, 1 mm. Al, H.V.L. 7.6 mm. Cu; Output 50 r/min. with B.S. for 10×10 cm. field.

1939–48: 1,000 kV, 4.5 ma., 100 cm. F.S.D., filter 4.2 mm. Fe, 2 mm. Al, 2 mm. Pb, 2 mm. Al, H.V.L. 9.3 mm. Cu; Output 40 r/min. with B.S. for 10×10 cm. field.

During this later period a few cases were treated at 1,000 kV 70 cm. F.S.D., filter 4.2 mm. Fe, 4 mm. Al, H.V.L. 7.6 mm. Cu with a dosage rate of 200 r/min. This was done to see whether there was any advantage in operating at high dosage rate levels [6, 7], but the complication of varying other physical factors to obtain the necessary high dosage rate made the results difficult to assess. It is hoped with the modified target to operate at 12 kW, when the necessary high intensity will be available at 9.3 mm. Cu H.V.L.

The output from the tube operating at a million volts and 4.5 ma. is equivalent to that which would be obtained from 7 kilograms of radium under the same conditions and the beam wavelength is approaching that of gamma rays.

PHYSICAL ADVANTAGES

Depth dose.—The main physical advantage in operating with million-volt X-rays, when compared with the usual 250,000 volts X-rays, is the gain in depth dose; that is the dose at a depth relative to the dose at the surface. For comparison, consider the usual therapeutic conditions and our own, for a beam of 10×10 cm. and at 10 cm. depth.

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If we give an *air* dose of 100 r under each condition (fig. 3), the total dose at 10 cm.

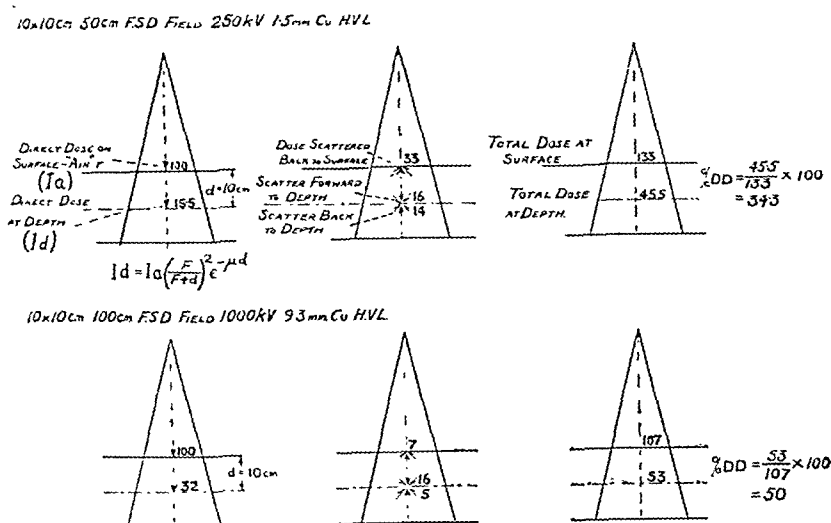


FIG. 3.—Composition of dose at depth, at 250 and 1,000 kV.

deep at 250 kV is 45.5 r and at a million 53 r, a gain with a million, but not a great one. However, the shorter the wavelength of the X-rays used, that is the higher the kilovoltage employed, the more forward becomes the scatter from the absorption processes. Therefore at 250 kV, there is considerably more scatter back to the surface than there is at a million. The result is that the surface doses are 133 r and 107 r respectively. This gives percentage depth doses, that is the doses at the depth as a percentage of the surface doses as 34.3 and 50% respectively, representing a gain of about 50% in the dose at the depth by employing million-volt X-rays.

Now consider how this happens apart from the effect of the large difference in surface backscatter. The dose at a depth can be regarded as being made up of three components (fig. 3); first, the direct or through dose, comprising the primary rays which penetrate right through the patient to the depth and are absorbed there; secondly, forward scattered rays, scattered from the part of the patient above the level of measurement; and thirdly, backscattered rays, scattered back from the part of the patient below the level of measurement.

At 250 kV the direct component at 10 cm. depth is only 15.5 r while at a million it is 32 r. This great difference is due to the higher penetration of the million volt rays. Not only this, but the direct component is nearly $\frac{2}{3}$ of the total dose at the depth at a million volts, whereas at 250 kV it is only approximately $\frac{1}{3}$. Therefore if the direct component

The output from the tube operating at a million v a reduction of the dose necessary to that which would be obtained from 7 kilograms of the lungs. conditions and the beam wavelength is approaching that gained from the increased depth

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Depth dose.—The main physical advantage when compared with the usual 250,000 v is the dose at a depth relative to the usual therapeutic conditions at 10 cm. depth.

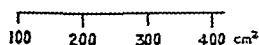
Field size cm. × cm.	Maximum separation 250 kV. 10°V.	
5 × 5	5.5 cm.	9.5 cm.
10 × 10	8.4 cm.	12.2 cm.
20 × 20	12.0 cm.	14.1 cm.

The usual conditions 1 mm. Cu H.V.L.
F.S.D.

Our conditions ?

If we give an air dose

10 × 10 cm. 50 cm. F



Graph.) Maximum separation between two opposed fields, up to which the central dose is equal to or greater than the skin dose.

obtained by the employment of supervoltage X-rays, there are two other factors that should be mentioned.

Variation of transmission through body components.—Recently, we have made measurements of the transmission and scattering from fresh post-mortem specimens of various components of the human body. Considering here primarily the effect on X-ray beams of H.V.L. 1.5 mm. Cu and 9.3 mm. Cu (250 and 1,000 kV) we obtain the results shown in the second and third columns of fig. 6. The figures in the table

SPECIMEN	RATIO		
	Transmission through specimen Transmission through water of same depth		
	250 kV		1,000 kV
	1.0 mm. Cu H.V.L.	1.5 mm. Cu H.V.L.	9.3 mm. Cu H.V.L.
Muscle, water, brain tissue, standard presswood	1.0	1.0	1.0
5 cm. thick, "aerated" lung ..	1.47	1.43	1.32
3.7 cm. thick, fat	1.06	1.04	1.02
3.5 cm. thick, body of vertebra ..	0.93	0.95	0.98
0.55 cm. thick, rib	0.91	0.925	0.98
0.7 cm. thick, skull	0.87	0.90	0.97
4 cm. thick, shaft or head of femur	0.82	0.86	0.95

FIG. 6.—Relationship between the transmission through human body components at 250 and 1,000 kV.

represent the ratio of the transmission through the specimens, compared with the transmission through the same thickness and shape of presswood which we see has the same transmission as water, muscle and brain tissue down to at least 0.15 mm. Cu H.V.L. Some of the results are rather surprising. The vertebra for instance at 250 kV only causes an excess loss of 5% while at a million it is 2%. Presumably this loss is low because there is really little dense bone in the vertebra. On the other hand ribs, skull and in particular femur, cast appreciable shadows across our 250 kV beams, while at a million volts the shadows are practically negligible.

It has long been realized that our isodose plans, as has been emphasized by Spiers [8, 9], make no allowance for these extra absorptions. Just how our results can be applied to this planning is not simple. From preliminary experiments it would appear that an approximate idea of the depth doses in the "shadows" can be obtained by

can be increased by some of the Royal Society of Medicine greater value at a million volts

to $\left(\frac{F}{F+d}\right)^2 e^{-\mu d}$ and in this modification to the tube in 1939, the tube has operated and until the middle of 1947 it had not been dismantled.

F.S.D. is the only variable. The factor of the electrodes, so that a new type of target could be applied, since a slight instability had appeared, which application of voltage every Monday morning.

appreciably up to F equal to 100 cm., so as the surface of the nose of one of the intermediate percentage depth dose at a million volts will be electrode. Tube filaments, of which there the effect will be small. Investigating the scatter of a flat-faced target, on an average, has been at 10 cm. depth, they total 30 r and at a million volts

$\frac{1}{3}$ of their respective total doses at the depth. Therefore, three months, but during the in the amount of scatter will produce a greater effect on the floors three times, and part than it will at 1,000 kV. The scatter component at any one of the food water supplies were the volume of material irradiated, which for a fixed F.S.D. and time, whereon repairs are made, varies with the field size. Therefore alteration in the field size will increase the scatter and hence the depth dose much more than it will

volts. This means that at a million volts there will be very little loss in dose and whether with very small fields compared with the depth dose for medium and malignant while at 250 kV, as we all know, there is a very marked falling off in depth dose was re-

the small fields. Fig. 4 shows the very appreciable gain in the dose delivered to any depth at a million volts when compared with that delivered at 250 kV for the same surface dose

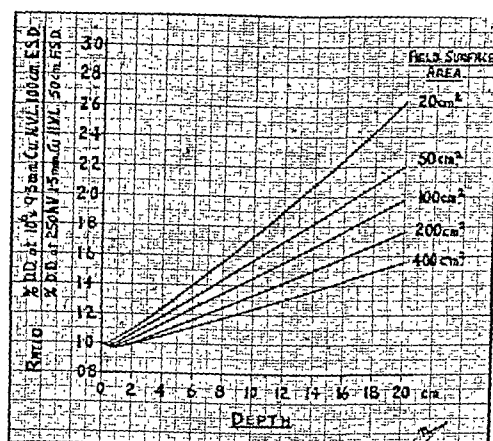


FIG. 4.

cases. It will be seen that the gain is maximum for the smallest fields at the greatest depths, e.g. for a 4×5 cm. field, the gain in the dose at 10 cm. depth is as high as 72%.

Opposed fields.—A common misconception is that with the increased depth doses obtained at a million volts, there will be a reduction in the effectiveness of treatment by opposed fields. That this is not the case is illustrated in fig. 5, in which the curves give the maximum separation between two opposed fields by tissue, up to which the dose at the centre of the tissue is at least equal to the skin dose. For a 5×5 cm. field at 250 kV this is 5.5 cm., while at a million volts it is 9.5 cm., a considerable gain in the permissible separation, making possible the treatment of a number of sites by the simple and accurate method of opposed fields. Further, in the treatment of cases like the œsophagus where the main dose is obtained by two opposed fields and the supplementing glancing fields pass through vital organs, the increased effectiveness

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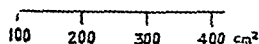
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multiplying our standard depth doses for water by the factors given in fig. 6 or 7.

The figures for lung were obtained with the lung aerated to a pressure representing the mean negative pressure it would be subjected to in the living body. Its absorption under these conditions makes it equivalent to half its own thickness of muscle tissue over the whole range of wavelengths investigated.

From these results it can be said that generally with million-volt X-rays our actual dose distributions in the patient are very nearly the same as those calculated

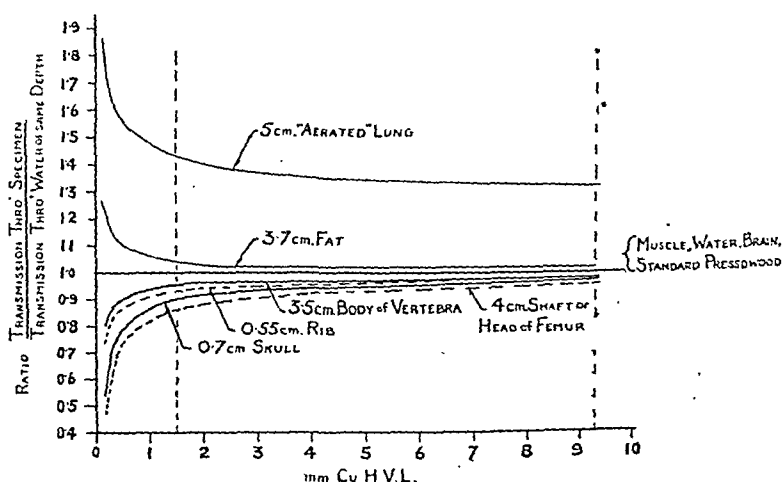


FIG. 7.—Relationship between the transmission through human body components and water, for different qualities of X-rays.

from our phantom isodoses irrespective of whether the beams have to pass through bones. On the other hand at 250 kV, if possible the beams should be routed away from bones, particularly of the compact type, in order to avoid an appreciable loss in depth dose, of unknown value, and also possible detrimental clinical effects on the irradiated bone by its relatively high absorption. Finally, it should be noted from comparison of columns one and two of fig. 6 that there is an appreciable reduction in the relative transmission of bone when the 250 kV tube is used with light filtration such as that produced by a H.V.L. of 1 mm. Cu, indicating that the maximum economical filtration should always be used.

IONIZATION LEVELS

Following the measurement of the transmission by different body components at various X-ray wavelengths, it was thought that there might be different ionization intensities in the superficial layers of the patient and near heavy absorbing media such as bone. These might be of clinical significance.

Ionization in the superficial surface layer.—A chamber of tissue equivalent walls, with a front wall $25\ \mu$ thick, was built into a presswood phantom (fig. 8). With the addition of tissue-equivalent material to the thin wall of the chamber, the ionization current in the chamber per r will indicate the ionization occurring in tissues just beyond the thickness of tissue above the chamber.

The two conditions investigated so far have been, as nearly as possible, those under which the skin reactions have been compared, namely:

250 kV, 1.85 mm. Cu H.V.L., 53 cm. F.S.D. with an 8×8 cm. field defined by a 50 cm. F.S.D. wooden-ended applicator, and 1,000 kV, 9.3 mm. Cu H.V.L., 100 cm. F.S.D. with an 8×8 cm. field defined by a diaphragm at approximately 45 cm. F.S.D.

In fig. 8 the ionization curves are plotted, in each case, as percentages of the peak ionization observed as the front wall of the chamber was thickened. At a million volts and the minimum front wall of 0.025 mm. thickness, the ionization was only 67% of the peak value which occurs with 1.0 mm. depth. However, the increase of ionization is rapid so that with 0.2 mm. depth the ionization is 90% of the peak value.

At 250 kV, however, the ionization is nearly at its peak with the minimum wall of 0.025 mm., reaching full saturation at 0.2 mm. depth. Not only this, but if the applicator end had been in contact with the chamber top surface, as it would have been

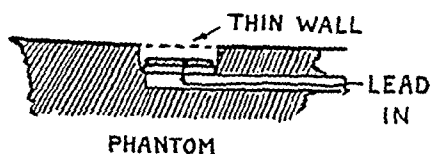
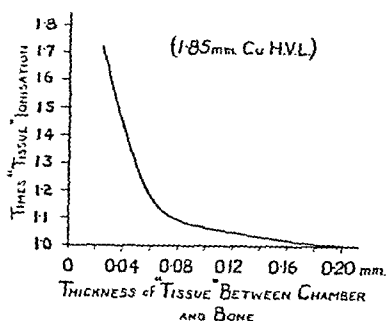
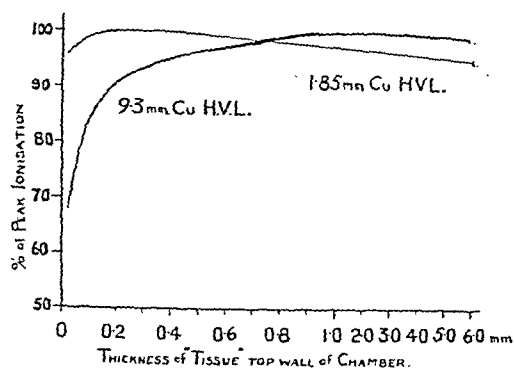


FIG. 8.—Ionization with depth in "tissue" as a percentage of peak ionization.



FIG. 9.—Effect of bone above chamber.

clinically, peak ionization would already have been attained, the applicator end acting as the saturator.

Therefore in the two clinical conditions compared, there is an appreciable difference in the level of ionization in the superficial layers and hence in the energy absorbed in these layers (under the physical conditions used, the relative energy absorption in tissue, per ion pair produced in air, only differs by some 3%). The clinical significance of this information will be indicated in Dr. Jones' paper.

Ionization near bone.—Since bone contains elements of medium atomic number, there is some photo-electric absorption with 250 kV X-rays, but very little with 1,000 kV rays. It was therefore expected that there would be a considerable difference under the two conditions in the ionization levels per r in the superficial tissues surrounding bony structures. To examine this, the thin wall chamber in its phantom was covered by 13 mm. of tissue-equivalent material and 1 mm. of bone. By traversing the bone through the tissue and observing the alteration in the ionization produced in the air of the chamber, we have an indication of the ionization produced in the tissue at a distance from the bone just greater than the thickness of tissue-equivalent material, intervening between the bone and the air of the ionization chamber.

At a million volts only 2% extra ionization could be detected and the effect of the bone on the surrounding tissue is therefore negligible. At 250 kV, however, the results as shown in fig. 9 indicate that the bone has a considerable effect on the level to which the superficial layers of tissue surrounding it are ionized. With between 13 mm. and 0.2 mm. of tissue between the bone and the chamber the ionization is constant, but as

the bone approaches closer to the chamber, the ionization current rises rapidly until with 0.025 mm. of intervening tissue the level is 72% above that with 0.2 mm. of intervening tissue. This means that tissue cells at this distance of 0.025 mm. from the bone receive 72% more ionization than that equivalent to the roentgen dose level estimated at that point. Extrapolating the curve it would appear that those tissue cells in contact with the bone probably receive as much as 130% excess ionization, while on the other hand the effect of the bone has disappeared in the tissues beyond 0.2 mm. from the bone.

It follows that at a million volts we need not worry about the increase in ionization in tissue around bone, as this is negligible, but at 250 kV we must remember that the ionization in tissue round bone may be as much as 2.3 times that indicated by the estimation of the dose there.

TREATMENT PLANNING

The treatment of every patient by the million-volt equipment has been regarded as a separate and individual problem requiring its own plan. The isodose plans (figs. 10 to 13) are those on the transverse sections of the patients through the centre of the treated volume. They illustrate a few representative methods of treatment of various sites, indicating particular points of interest and advantages gained by employing supervoltage X-rays.

Deep-seated lesions in large patients.—Applying the physical advantages which we have already discussed, it can be stated in general that at a million volts, due to the high depth doses for even small fields and the increased tolerance of the skin, a large dose of radiation can be delivered to a lesion no matter how deep-seated in the largest of patients. A typical case is:

Fig. 10, a carcinoma of the œsophagus.—In a patient of anteroposterior dimension of 23 cm., using the same six fields, an anterior, posterior and four glancing fields, the section shows, on the left, the isodose if treatment were carried out at 250 kV, 1.5 mm. Cu H.V.L., 50 cm. F.S.D.; and on the right, as it is done at 1,000 kV, 9.3 mm. Cu H.V.L., 100 cm. F.S.D. To deliver a dose of 6,000 r to the lesion at 250 kV, a dose of 4,000 r per field is required, resulting in a maximum skin dose of 5,000 r. It is doubtful if this could be accomplished. On the other hand, at a million volts only 2,760 r per field is required, giving a maximum skin dose of 3,530 r, 1,000 r below the dose which will produce a second degree erythema at this wavelength.

It will be noticed that at a million volts not only is it easier to attain a high lesion dose level, but also that the dose level falls off more rapidly in the normal tissue outside the lesion, a valuable factor in maintaining the patient's vitality during the treatment and convalescence.

TREATMENT OF LARGE SECTIONS

Carcinoma of the breast.—Fig. 11 shows the treatment plan for a very advanced carcinoma of the breast involving the posterior axillary skin fold, necessitating treatment of nearly one-third of the skin periphery. At a million volts, two opposed glancing beams were used, 29 cm. apart, resulting in a central deficiency of about 20% when compared with the maximum skin dose. This deficiency is readily corrected by the application of a "straight-on" central field which required only one-quarter of the dose given to the main glancing fields. As the dose to this field is low there is little extra irradiation of the lung.

At 250 kV employing opposed glancing fields [10], the dose at the centre of the lesion would only be about 50% of the maximum skin dose. A supplementary "straight-on" central field would not produce anything like uniformity throughout the section, since with the high dose required, and the rapid fall off in the field depth

There would be a very steep gradient in dose from the skin at the centre, to the edge of the field.

Comparison of the two diagrams shows the ease with which uniform irradiation can be achieved to large sections at million volts.

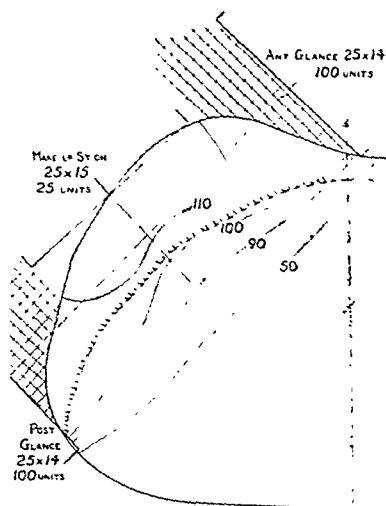
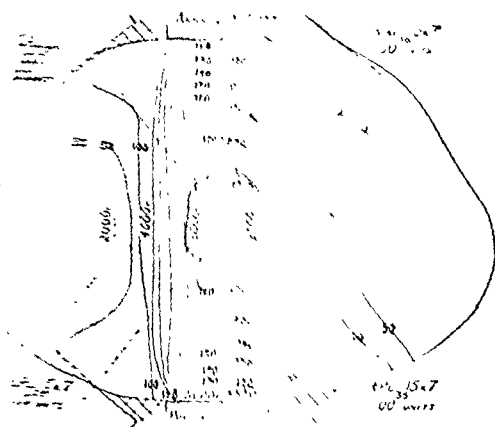


FIG. 10.—Ca. Breast L. (Longitudinal section).
Left: Treated by 250 kV, 100 cm. F.S.D.
6,000 r $D_T = 4,000$ r (100 r D_s).
Right: Treated by 10^6 V, 9.3 mm. F.S.D.
6,000 r $D_T = 1,000$ r (100 r D_s).
(Maximum possible 100 r D_s .)

FIG. 11.—Ca. Breast L. (Transverse section). Treated by 10^6 V, 9.3 mm. Cu H.V.L., 100 cm. F.S.D.

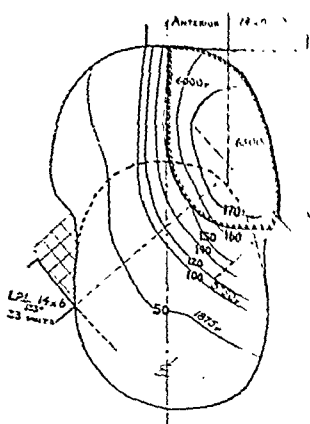


FIG. 12.—Ca. Faucial Pillar. R
100% = 3,750 r.

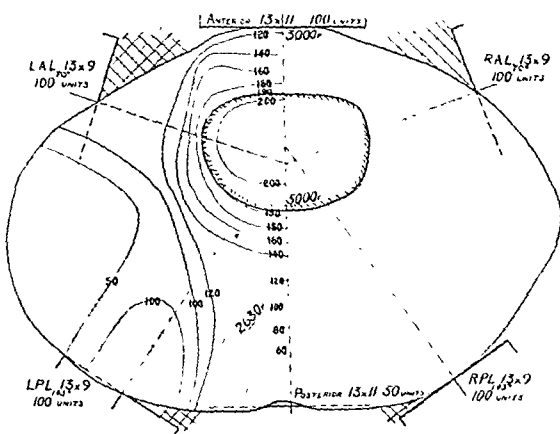


FIG. 13.—Ca. Bladder. Treated by 10^6 V, 9.3 mm. Cu H.V.L., 100 cm. F.S.D.

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In this group of cases the high depth doses available at a million volts are used to permit either a reduction of the dose to fields passing through vital organs or employment of a plan in which the beams do not take the most simple and economic route to the lesion, but are directed to avoid irradiating a vital organ.

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the bone approaches closer to the chamber, the ionization current rises rapidly until with 0.025 mm. of intervening tissue the level is 72% above that with 0.2 mm. of intervening tissue. This means that tissue cells at this distance of 0.025 mm. from the bone receive 72% more ionization than that equivalent to the roentgen dose level estimated at that point. Extrapolating the curve it would appear that those tissue cells in contact with the bone probably receive as much as 130% excess ionization, while on the other hand the effect of the bone has disappeared in the tissues beyond 0.2 mm. from the bone.

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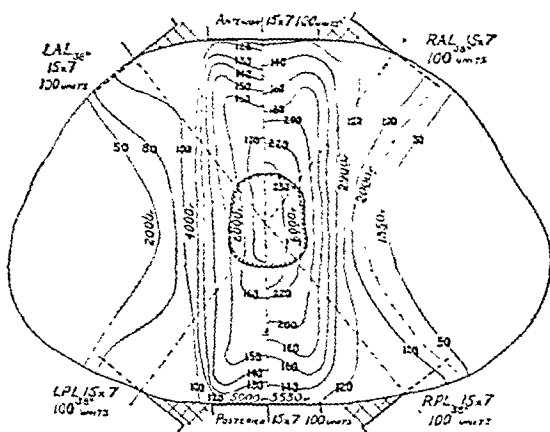


FIG. 10.—Ca. Esophagus.

Left: Treated by 250 kV, 1.5 mm. Cu H.V.L., 50 cm. F.S.D.
 $6,000 \text{ r D}_T \equiv 4,000 \text{ r/field} \equiv 5,000 \text{ r D}_S$.
 Right: Treated by 10^6 V , 9.3 mm. Cu H.V.L., 100 cm. F.S.D.
 $6,000 \text{ r D}_T \equiv 2,760 \text{ r/field} \equiv 3,530 \text{ r D}_S$.
 (Maximum possible = 7,600 r D_T.)

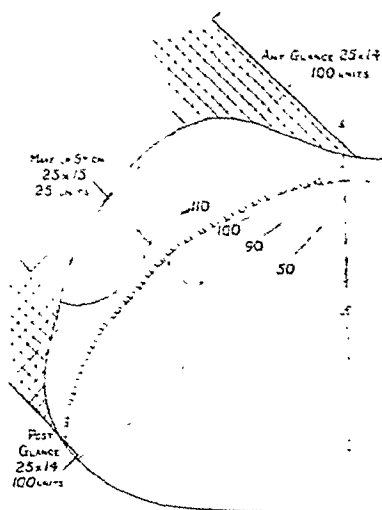


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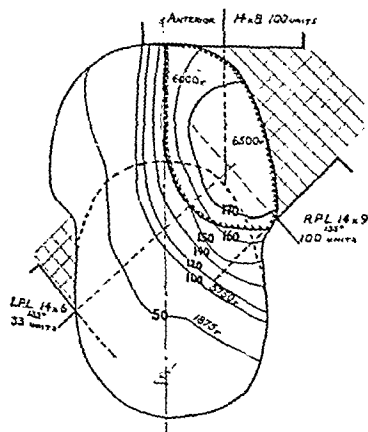


FIG. 12.—Ca. Facial Pillar, R.
 $100\% = 3,750 \text{ r}$.

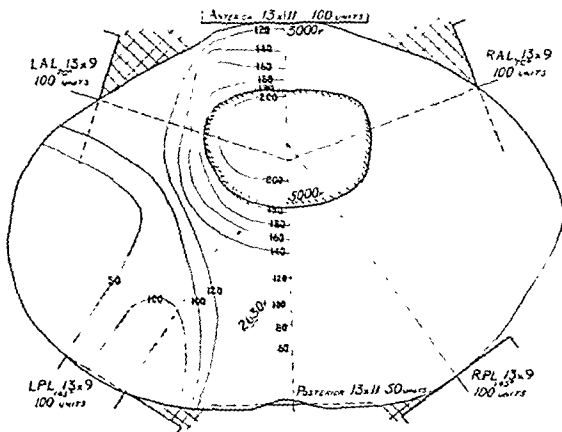


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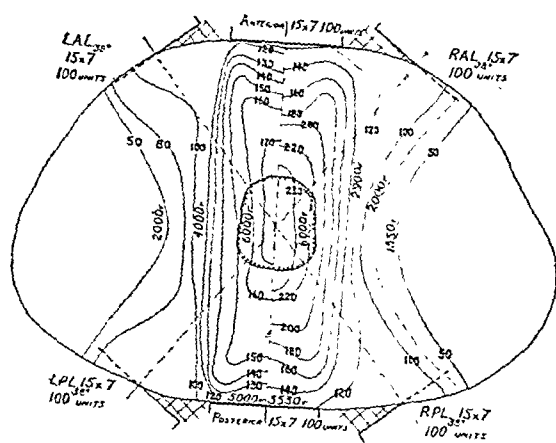


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6,000 r $D_r \approx 2,760$ r/field $\approx 3,530$ r D_s .
(Maximum possible = 7,600 r D_r .)

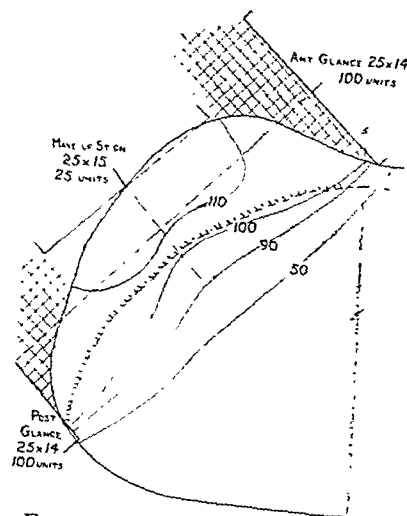


FIG. 11.—Ca. Breast L. (Transverse section). Treated by 10^6 V, 9.3 mm. Cu H.V.L., 100 cm. F.S.D.

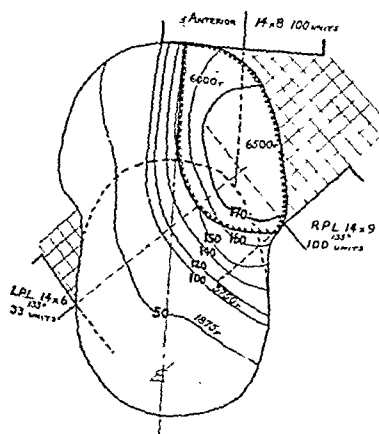


FIG. 12.—Ca. Faucial Pillar, R.
100% = 3,750 r.

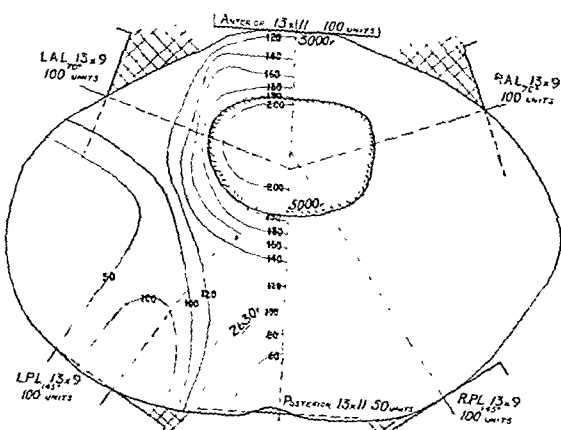


FIG. 13.—Ca. Bladder. Treated by 10^6 V, 9.3 mm. Cu H.V.L., 100 cm. F.S.D.

REDUCTION OF DAMAGE TO VITAL ORGANS

In this group of cases the high depth doses available at a million volts are used to permit either a reduction of the dose to fields passing through vital organs or employment of a plan in which the beams do not take the most simple and economic route to the lesion, but are directed to avoid irradiating a vital organ.

Carcinoma of the fauces, unilateral.—In the case in fig. 12 the general line of approach at 250 kV would be by two lateral fields, damaging all the salivary glands and leaving

the patient with a permanently dry mouth. At a million volts the treatment can be effectively carried out by an anterior field and a posterior glancing field on the diseased side, with a small supplementary posterior glancing field from the other side to increase the dose in the postero-medial part of the lesion. This supplementary field only requires a dose of one-third that applied to the main fields, and is so aimed as to miss the salivary glands on the unaffected side. The result is that the salivary glands receive less than one-third of the lesion dose, a dose which does not cause functional damage.

Carcinoma of the œsophagus.—In the case of carcinoma of the œsophagus (fig. 10) we have already indicated the great increase in tumour dose per field r with the employment of supervoltage X-rays. This gain can be usefully employed in permitting a reduction of the dose applied to the glancing fields commensurate with the delivery of the necessary tumour dose. This reduction to the dose level of the glancing fields reduces the lung irradiation and damage.

Carcinoma of the cervix.—In order to avoid bladder and rectal upset in the treatment of this condition, the major portion of the dose to the lesion is delivered through four glancing fields, with an anterior and posterior field each receiving only one-half of the dose applied to each glancing field. The result is an isodose of the shape required with a fairly rapid fall off anteriorly and posteriorly, so reducing the radiation effects on the bladder and rectum to a level much below that which would occur if full dosage had been applied to the anterior and posterior fields.

Carcinoma of the bladder (fig. 13).—In this case the patient was enormous, with an anteroposterior measurement of 26 cm. and a width of 37 cm. Nevertheless it is possible with an anterior and four glancing fields, supplemented by a posterior field raised to only one-half the dose of the others, to deliver a maximum dose of 7,500 r to the bladder lesion, if required. The application of only one-half the dose to the posterior field effectively lowers the dosage level to which the rectum is raised, so diminishing the likelihood of proctitis.

LESIONS OF SMALL CROSS-SECTION

Carcinoma of the rectum.—(For the isodose distribution see fig. 94, p. 128, *Supervoltage X-ray Therapy*, by R. Phillips, London.) In this case the lesion was of small cross-section, 5 cm. diameter. The plan shows on the left the isodose at 250 kV, and on the right at 1,000 kV when ten 8 cm. wide fields are employed in both cases. The most prominent feature is the rapid fall off in dose outside the lesion at a million volts, compared with the relatively large block of tissue which is raised to the lesion dosage level at 250 kV. Secondly, the maximum skin dose is the same in both cases for the same field doses (200%) but the million-volt lesion dose is some 50% higher than that at 250 kV. It is not often that the lesion sections are so small or are enclosed by a longitudinal ellipsoid of such central cross-section, which this isodose implies, and it is now more common to use field plans with larger and fewer fields.

General.—It should be pointed out that in this survey of treatment isodose sections, no allowance has been made in the isodoses for the absorption of bone or the reduction of depth dose due to lack of scatter from lung. Both of these will have a detrimental effect on the 250 kV isodoses but little effect at 1,000 kV. This would even further emphasize the advantages of the million-volt radiations.

Summary of the Physical Treatment Advantages of 1,000 kV X-rays

Due to the increased depth doses, other physical factors and reduction in the skin reaction, the following advantages are obtained:

(1) Fewer fields can be used to deliver the lesion dose required and hence we obtain a simplification of the treatment plan with a resulting gain in accuracy.

(2) Alternatively we can reduce the dose level to some or all of the multiple fields.

(3) It is possible either to reduce the dose on fields passing through easily upset organs or alternatively in some cases to avoid irradiating them altogether, attaining the necessary tumour dose by a less efficient routing of the beams to the lesion.

(4) In nearly all cases, 6,000 r can be delivered to the lesion in five weeks, no matter how deeply seated it is or how large the patient.

(5) By careful planning the dosage level can be made to fall off rapidly outside the volume to be irradiated, reducing the ill-effects on the patient.

(6) It will be noticed that no attempt is made to avoid beams passing through bony structures, since bone absorption at a million volts is very little greater than tissue, with the result that the isodose plans are a very near approach to the actual dose distribution in the patient, irrespective of whether bone is present or not. Also round the bone there is only a negligibly small trace of ionization in excess of that indicated by the r dosage level of the isodose. On the other hand at 250 kV the shadow effect of the bone is high, and the ion density around bones may be as much as twice the level inferred by the r dose level indicated by the isodose. This may be of clinical significance.

In this note it has only been possible to deal with some of the physical aspects of treatment at a million volts, and many of the isodose plans have had to be omitted; other physical aspects will be mentioned in Dr. Jones' paper.

Before closing, I should like to express my indebtedness to my ex-colleagues at Messrs. Metropolitan Vickers, whose enthusiasm made such an equipment possible; in particular to Mr. T. C. Crichton who was responsible for the erection of the equipment, and who has made the instruments necessary for the experimental work reported herein; to our Pathology Department, especially Dr. Cureton, who supplied the pathological specimens; to the eight Medical Officers with whom I have had the pleasure of working on the million volt equipment, I can only say "thank you" for the understanding way they have helped with the physical treatment problems, making treatments in effect a combined operation of medical and physical knowledge.

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Clinical Reactions and Injuries in Supervoltage Therapy

BY ARTHUR JONES, M.D., M.R.C.P.

THE following is a brief account of the clinical effects of supervoltage radiation as we have observed them, and of the injuries which have resulted during the treatment of malignant disease with the million-volt apparatus.

The extension of the roentgen unit of X-ray dosage has enabled clinicians to compare the biological reactions produced at different photon energies, and it is a matter of general experience that to produce a given skin reaction requires a larger dose of gamma radiation than of X-rays. It is commonly agreed that if 600 r of X-rays at

200 kV is required to produce a standard erythema, then about 1,000 r of gamma radiation is needed to give this same response (both doses being stated "with back-scatter"). A voluminous literature, much of it empirical, has accumulated about this variation of skin response with radiation quality, and the advent of million-volt X-rays, intermediate in mean energy between the "deep therapy" range and gamma rays from radium, gave promise of elucidating the problem. Early experiments by Phillips (1944) confirmed the theoretical supposition that the *threshold* erythema dose was some 50% higher at one million volts than at 200 kV, but further experiment was difficult, since it was unjustifiable to treat superficial lesions with this penetrating radiation, and treatment of malignant disease was by fractionation of the dosage. Here was encountered, as in its wider context, "the opportunity fleeting; experiment dangerous, and judgment difficult". However, one definite observation has been that the skin dosage for a second degree erythema, by fractionation over three to five weeks, is between 4,000 and 5,000 r. The erythema develops more slowly than at 200 kV, reaches its maximum later, and takes longer to subside.

The mechanism of this differential threshold with wavelength has been attributed by some to the different absorption processes, whereas others regard it as a true function of photon energy. The experimental determination of maximal ionization depth by Innes provides some new light on the problem (*see* fig. 8 in Mr. Innes' paper). Since the depth of the basal layer and subpapillary vascular plexus in the skin is some 0.2-0.4 mm., it will be seen that the maximal ionization at one million volts occurs measurably below this level, whereas with the 250 kV beam saturation has already occurred in the wooden end of the applicator on the skin surface. This will account for a difference of over 7½% in local energy absorption. The absence at one million volts of the photo-electric absorption process by the sulphur in the superficial skin strata accounts, according to Gray (1940), for some 13% difference in ionization. These two effects taken together may account for 20-25% of the difference in energy absorption, and it cannot yet be ruled out that the remaining difference in skin reaction is not an inherent function of the quality of the beam.

MUCOSAL REACTIONS

In the "deep therapy" range of X-rays the factor limiting radical treatment is often the severity of the skin reaction, but the penetrating properties of a million-volt beam may produce a deep mucositis in the region of the tumour and thereby effectively limit the amount of radiation permissible. This is best seen in two sites: (a) in the mouth, pharynx and larynx, and (b) in the pelvis.

During irradiation of the oropharynx by a fractionated dose method, reddening of the mucous membrane develops between the tenth and fifteenth day. A few days later a white fibrinous membrane appears, and if heavy dosage is used the membrane may become quite thick; it is adherent, and bleeds like a diphtheritic membrane if its premature removal is attempted. During the mucositis the patient has sore throat, cough, dysphagia and dryness of the mouth. The mucosal reaction always precedes the skin reaction; it subsides about three weeks after the end of treatment, but the dryness of the mouth may last for months. The skin reaction, developing later than the mucositis, also takes longer to resolve. In a few cases of post-cricoid and pharyngeal irradiation, gastrostomy has been required during treatment, and one or two of the laryngeal and thyroid cases have required emergency tracheotomy.

In the pelvis, the mucosal reactions may affect the rectum, the bladder and the vagina, and in treating one of these organs the methods described by Mr. Innes are used to minimize the dose received by neighbouring structures. Irradiation of a rectal tumour commonly produces a proctitis starting at the end of the first week of treatment, manifesting itself by tenesmus and watery diarrhoea; it is rarely severe enough to interrupt treatment, but it adds to the patient's discomfort. Proctitis of

less severity may occur during irradiation of the ovaries, uterus, parametrium, prostate and bladder.

Cystitis occurs in most cases of pelvic irradiation at about the eighth day, but the dysuria and frequency of micturition merely inconvenience the patient, and are partly relieved by alkaline mixtures containing hyoscyamus. Transient vaginitis may be mentioned as occurring similarly, but it produces no disability.

These mucosal reactions have proved to be the major burden which patients with malignant disease have had to bear during their course of supervoltage therapy. Soreness of the mouth and dysphagia may render an out-patient's life a misery, and it is necessary to have the patients in hospital for symptomatic treatment during the active phase of the mucositis.

There is one other aspect of mucosal reaction which I would like to mention. In a number of cases, especially in the pharynx and œsophagus, the mucositis has been unduly severe, and has limited the dose administered to perhaps 3,000 r in three weeks instead of the planned 4,000 or 5,000 r in five weeks. In a few of these cases, the ultimate result has been unexpectedly good—it is as though some factor common to both tumour and its mucosal bed has enhanced both the radiosensitivity and the radiocurability of the lesion. Experience had previously shown that the curative dose in these cases would have been quite inadequate in the absence of this "flare" reaction. This aspect of tumour response appears worthy of further biological study.

GENERAL REACTIONS

It was claimed by American workers in the early days of supervoltage therapy that the general reactions in the patients were less severe than at the "deep therapy" range. The physical investigation of total energy absorption has shown that the integral dose, expressed as gm. r per r on surface, rises with increase in the half-value layer of the beam, so that at H.V.L. 9 mm. Cu it is some 11% greater than at H.V.L. 2 mm. Cu. This integral dose has been given as *per r on surface*. For a given deep tumour dose, however, the integral dose at one million volts is considerably less than at 250 kV. The implications of this are shown in fig. 1. The benefit derived may be seen in Table I of the comparison of the integral doses in treating a case of

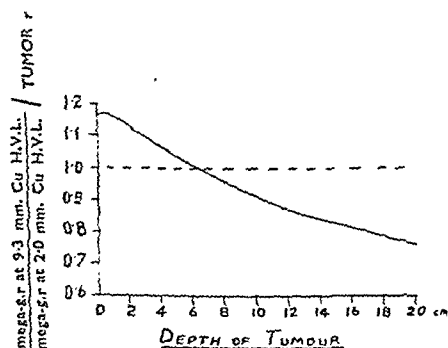


TABLE I.—COMPARISON OF INTEGRAL DOSES IN RADIOTHERAPY OF RECTAL CARCINOMA

Date	1,000 kV	200 kV
Lesion-dose (5 weeks)	6,000 r	6,000 r
Dose per field ..	1,620 r	2,400 r
Dose per day ..	650 r	960 r
Maximum skin dose	3,400 r	5,030 r
Integral dose ..	40 m.-g.r	65 m.-g.r

FIG. 1.—Relationship between integral dose at 1 M.E.V. 9.3 mm. Cu H.V.L. and 250 kV 2.0 mm. Cu H.V.L. when delivering the same tumour dose. Field 10 × 10 cm. 100 cm. F.S.D. Patient 20 cm. thick.

carcinoma of the rectum. (The figure of 40 Mega-gm. r is nearing the limit of tolerance.) While radiation sickness does occur in patients undergoing supervoltage therapy, it is probably less frequent than at 250 kV. Considering the extent of the lesions treated and the total tumour doses given, it can be concluded that the general reactions are less severe in the supervoltage range.

Blood changes have followed closely those occurring at the deep therapy range. In one respect, however, there has been a definite advantage in using the million-volt tube. This has been in the treatment of localized mediastinal masses in certain cases of reticulosis in which "deep X-ray" therapy had resulted in a dangerous leucopenia and radiation therapy had been abandoned. The use of small fields with the million-volt apparatus enabled us to deliver an adequate lesion dose before severe blood changes supervened.

INJURIES FROM SUPERVOLTAGE RADIATION

When the Year Book of Radiology for 1937 recorded the opening of the Mozelle Sassoon Department at St. Bartholomew's Hospital, the Editor observed: "Presumably the operators of the new plant will familiarize themselves with the not always happy effects of such high-voltage radiation by conferring with their American colleagues before starting therapy on a large scale". This statement is a reminder of the unfortunate injuries and necroses which occurred in America in those early days, before the dosage distributions and other potentialities of supervoltage apparatus were fully appreciated.

We can record that relatively few severe injuries have occurred at Bart's and this is a tribute to the careful planning of each individual case by Mr. Phillips and Mr. Innes, and also to their care in setting up each patient for treatment, when several small fields are in apposition and each exit dose has to be considered.

(a) *Injuries to skin and subcutaneous tissue.*—The early skin reactions already described have often left a mild chronic radiodermatitis as sequel. Telangiectasia is not uncommon and, as at 200 kV, appears more frequently after daily doses of 500 r on the skin than if each skin dose is limited to 300 r per day. Mild skin atrophy is less common than at 200 kV but intracutaneous fibrosis and œdema, giving a leathery skin, are more common. Similarly, subcutaneous fibrosis, especially in fatty tissue (e.g. buttocks), is more common with supervoltage. This would accord with the observations on the depth at which maximal ion density occurs—the endarteritis is occurring mainly in the deep vascular plexus and not in the subpapillary plexus.

Of all the 800 cases treated, in only 12 has true late radiation necrosis of skin and subcutaneous tissue occurred. One of these was a small pre-auricular necrosis following the irradiation of a recurrent parotid tumour which had actually shown chronic radiodermatitis from previous 200 kV irradiation when first treated. The other cases all followed pelvic irradiation—6 cases of rectal carcinoma and 5 of anal canal carcinoma. The 6 necroses out of 192 cases of rectal carcinoma is a small figure, and in 4 of these the precipitating factor was obvious—two had had re-treatment at 1,000 kV after previously having had a full course of treatment; one had a subsequent radium implantation; one other had gone to another hospital and, without divulging his previous history, had been re-treated at 200 kV. Two of these rectal patients with necroses are alive and comparatively well (figs. 2 and 3).

The incidence of necrosis in anal canal carcinoma is unfortunately quite different—out of 23 patients treated, 5 developed necroses. Treatment of the anal growth was by anterior, posterior and oblique fields, supplemented by a perineal field, the maximum skin dose being 4,200 to 4,600 r on the posterior perineum; one case had interstitial radium at another hospital later; and one case had had a maximal skin dose of 5,250 r to the perineum. It is of interest that, although in rectal cases the perineal skin has received a similar maximal dose to that given to the anal cases, necrosis has been rare in comparison with the anal series. The tumour response in anal carcinoma has been excellent, and it would appear that the high incidence of necrosis here is due to failure of the normal repair processes in a heavily irradiated, moist and perhaps schæmic field, which has already been the site of ulceration.

(b) *Injuries to connective tissue.*—The deep mucosal reactions already described are occasionally followed by late fibrosis in the organs concerned. This has been most common in the rectum, where clinically recognizable fibrosis was present in 30 of the 192 cases treated; but in very few was it of such severity as to necessitate colostomy

for stricture. One uterine case was followed by persistent rectal ulceration and fibrotic stricture requiring colostomy.

One case of rectal carcinoma is of considerable interest because of the sequel of pelvic fibrosis. A man of 42 had a partial removal of a Stage 2 adenocarcinoma of the lower third of the rectum, followed by X-ray therapy at 1,000 kV-4,500 r to the tumour in four weeks. Six months later he developed a posterior perineal radionecrosis which healed in eight months. Soon afterwards he had enlarged inguinal glands, which were treated to 4,500 r in each groin. The patient became symptom free and returned to work, but eight months later was admitted with anuria to another hospital

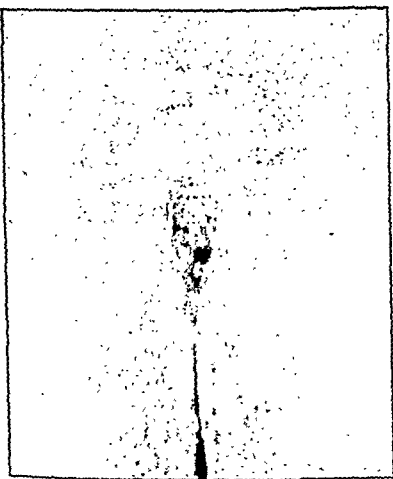


FIG. 2.—Necrosis at upper end of natal cleft following supervoltage irradiation of stage 3 rectal carcinoma in 1943 (tumour dose of 5,000 r in twenty-seven days; maximal skin dose 5,600 r in posterior perineum). Colostomy, 1942. Patient is well, with no evidence of active growth, in 1948.

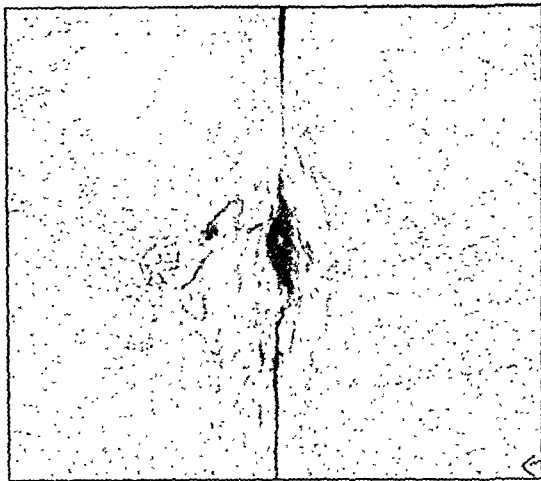


FIG. 3.—Necrosis in natal cleft following supervoltage irradiation in 1945 of a recurrent rectal carcinoma (originally treated by perineal excision and colostomy in 1944). Tumour dose of 3,350 r in twenty-two days, followed ten weeks later by 2,000 r in eighteen days; maximal skin dose 5,600 r on posterior perineum. The patient leads a busy life and has no evidence of active neoplasm in 1948.

and died in uræmia. Autopsy showed no evidence whatsoever of rectal growth, but he had pelvic fibrosis, bilateral hydro-ureters, hydronephroses and pyelonephritis.

Brachial neuritis followed irradiation of the supraclavicular and axillary region in one case of mammary carcinoma.

(c) *Muscle fibrosis*.—This has occurred mainly in the neck, where platysmal and sternomastoid fibrosis has followed irradiation in 3 out of the 15 cases of thyroid carcinoma. The only disability resulting has been slight restriction of neck extension.

(d) *Respiratory tract*.—Persistent laryngeal œdema with fibrosis has been noted in 6 cases—one being in thyroid, one in post-cricoid, and 4 in laryngeal irradiation; in one of these latter, the œdema masked a perichondritis and necrosis of the cartilage. 5 of these cases ultimately required tracheotomy, and one needed gastrostomy also.

Apical pulmonary fibrosis has been noted in one case of thyroid irradiation, and in one case of œsophageal carcinoma the patient died of massive fibrosis of both upper lobes one year after the X-ray therapy. Lung fibrosis has, of course, been relatively common in the cases of bronchial carcinoma; but with the exception of one case has been overshadowed clinically by the primary neoplastic condition.

(e) *Œsophagus*.—Irradiation of the œsophagus has resulted in rather dramatic sequelæ in two cases:

OCT.—RADIOL. 2.

(1) A man of 59 was given supervoltage radiation to a squamous-cell carcinoma of the œsophagus (with mediastinal lymph-node involvement) at the level of the tracheal bifurcation. A tumour dose of 5,500 r was given in thirty-seven days, by a 6-field technique. Clinical improvement was excellent, but five weeks after irradiation the patient was admitted with mediastinitis and died two days later. Autopsy revealed a perforation into the right main bronchus (5×3 cm.). No growth was found in the necrotic mediastinal lymph-node mass, but microscopically there were a few carcinoma cells in the œsophageal wall.

(2) A man of 57 was given a tumour dose of 5,500 r in thirty-five days by 6 fields for an undifferentiated squamous-cell carcinoma of the middle third of the œsophagus. The clinical response was good, but two months later he died of a sudden hæmorrhage. At post-mortem there were no signs of growth, but œsophagus and aorta communicated through a large hole. There was no other evidence of necrosis above or below the perforation.

These two cases emphasize the view, put forward originally by Phillips, that here we are dealing, not so much with true necrosis, but with a failure of reparative processes by the normal tissues, after ablation of the growth. Possibly with some different method of fractionation, to minimize injury to the tumour bed, these unfortunate results might be avoided.

(f) *Bladder*.—There have been two cases of persistent hæmaturia from telangiectasia of the bladder wall—one, in a case of carcinoma of the bladder, which had a desquamative cystitis, was treated by total cystectomy (no growth was found in the operation specimen); the other, a case of carcinoma of the body of the uterus, has recurrent mild hæmaturia, but is otherwise well.

(g) *Bone*.—Two cases of bone necrosis—one of the mandible in carcinoma of the tongue, and one of the clavicle in carcinoma of the breast—have occurred, but showed no unusual features. Three of the cases of perineal necroses already described had involvement of coccyx and sacrum.

(h) *Eye*.—Conjunctivitis during treatment of carcinoma of the maxillary antrum has been unavoidable in treating certain cases, because of the anatomical extent of the growth. Of 18 antral cases treated, in 2 the conjunctivitis persisted, one other patient developed iritis, and 2 have X-ray cataracts.

(i) *Liver*.—Finally, a most unusual case of hepatic disorder has occurred during irradiation of a bronchial carcinoma. The patient, a Leading Aircraftsman, aged 24, had an oat-celled carcinoma of the right lower lobe bronchus diagnosed in the Middle East in June 1943 and treated by 2,200 r deep X-rays in Palestine (no further details available). He was treated at Bart's in October 1943 for persistent neoplasm by the million-volt apparatus. A tumour dose of 4,500 r was given in twenty-five days, followed by 2,400 r in five days to the right supraclavicular nodes, and then 775 r to the epigastric nodes in five days (with an 11×8 cm. epigastric field). His condition remained unchanged until mid-November 1943 when he became pyrexial and developed the rash of chickenpox. Radiation treatment was suspended. Thus the patient had been incubating varicella for half the total period of irradiation. The patient's condition deteriorated, and he died of pneumonia three days later. No clinical evidence of hepatic insufficiency had been observed. Autopsy showed, in addition to the bronchial tumour, a gross abnormality of the liver. The anterior surface of the right lobe was covered with petechiæ, and the upper part was intensely congested on section. The line of demarcation was at about the lower level of the anterior thoracic field of irradiation. Within the hyperæmic area there was intense active congestion of the liver sinusoids, chiefly *centrilobular*, with atrophy of liver cells; outside the congested area there were numerous areas of scattered *focal* necrosis.

This picture is unlike that previously described (e.g. Case and Warthin, 1924) in hepatic necrosis due to irradiation—the incidence of damage is stated to be usually peribiliary. The technique in this case differed in no way from that used in 3 other cases of bronchial carcinoma who suffered no ill-effects, and one can only conclude that some other factor, possibly the varicella, was involved in this case.

Such are the effects and injuries from supervoltage irradiation as we have seen them at St. Bartholomew's. The injuries, because of their relative rarity, have been described in some detail, and if any defence is demanded for the methods which have unfortunately produced them, one can only reiterate the Hippocratic aphorism of "extreme methods of cure for extreme diseases".

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Million-Volt X-ray Therapy

By I. G. WILLIAMS, F.R.C.S., D.M.R.E.

THIS report analyses the results of the treatment of malignant disease by means of X-rays generated at one million volts. As a primary research, five main sites were chosen: (1) Carcinoma of the breast, inoperable but without distant metastases. (2) Carcinoma of the cervix in all stages of the disease. (3) Cancer of the upper air and food passages. (4) Inoperable carcinoma of the rectum. (5) Carcinoma of the œsophagus—thus continuing a research into the results of X-ray therapy in malignant disease commenced in 1924 and elaborated in 1931. The research was, however, handicapped by the war; Mr. Ralph Phillips was the only therapist left in the hospital, and his time had to be divided between the million-volt and deep-therapy departments. Allocation of patients became dictated by the capacity of each department, and for humanitarian reasons patients not falling into the five groups were accepted for million-volt therapy. It has been the policy at St. Bartholomew's Hospital to treat early malignant disease by surgical rather than radiotherapeutic methods, if experience is favourable as judged by end-results. Thus patients referred for million-volt therapy were incurable by any other means, either because of the nature of the tumour, its anatomical extent or the general condition of the patient. Less than 5% of the total number fall into the early operable group. I think the tables are valuable as an indication of what we can and cannot do for our patients, in the conditions or stages in which they come to us for treatment. Our experience emphasizes clearly that early disease can be cured, that late disease cannot be cured, but that we can offer considerable palliation.

726 cases are available for study, no case has been eliminated and the figures are absolute values for those referred. We have been unable to trace a few of our patients, and these are counted as dead. As radiotherapists I believe we tend to over-emphasize our survival statistics. True, we have to present our successes as survival rates in order to compare with other forms of treatment or combined treatments, so as to give the patients the best possible chance of survival. But let us not lose sight of the degrees of palliation we can offer, the relief of physical and mental pain and distress, which cannot be recorded in graphs or statistics. When one remembers that less than 10% of malignant disease in all sites can be cured permanently, then the scope of radiotherapy as a palliative agent can be appreciated.

With these facts in mind, the following tables and remarks on the results of million-volt X-ray therapy in certain sites are presented.

Carcinoma of the Breast

Patients referred for million-volt therapy had advanced tumours, bulky primary growth and œdema of the skin, with extensive lymphatic metastases, often so large as

to be unsuitable and difficult for 200 kV therapy. A dose of 4,500 r can be delivered evenly to the chest wall, axilla and supraclavicular region in four to five weeks. This results in a brisk second-degree reaction which heals with fibrosis and later telangiectasia. There were no cases of pulmonary fibrosis resulting from treatment, but one patient developed a necrosis of the clavicle, and one patient has a fibrosis of the pectoral muscles, with a brachial neuritis, similar to the ones we used to get following radium implantation. Clinically, the primary tumour as well as large glandular metastases may disappear completely and histological examination of breasts removed after irradiation has shown either no recognisable carcinoma or degenerate carcinoma in fibrosed tissue. I can confirm Phillips' observation that disappearance of the primary tumour and regional lymphatic metastases is more certainly and more easily obtained with supervoltage than with deep X-ray therapy.

Total treated: 56.

Stages	No.	Dead	Alive		
(1) Operable	1	0	1	} 9/37 = 25%	} 9/50 = 18%
(2) Advanced or encephaloid	11	6	5		
(3) Inoperable	25	22	3		
(4) (Distant mets.)	13	13	0		
Recurrent	6	5	1		
					100% 46% 12% 0%

Stage 1: One patient. Refused operation. A/W 3 years. Dose: 4,500 r in 21 days.

Stage 2: Total: 11 patients. Two lactation carcinomas. Remainder: Breast or tumour too large to deliver an adequate dose with 200 kV therapy.

(a) Simple removal or biopsy and X-ray therapy.

7 cases. Alive 4 (8, 8, 6, 6 years).

Dead 3 (6½, 3, 1 year).

(1) Age 23. Encephaloid carcinoma in lactating breast—A/W 8 years. This patient developed a necrosis of the clavicle and the whole bone eventually sequestered.

(2) Age 26. Encephaloid carcinoma in a lactating breast. Alive 6 years.

(b) Radical mastectomy and post-operative X-ray therapy. 1 case died metastases at 14 months.

(c) X-rays alone. 3 cases. 1 A/W 3 years. 2 died at 1½ and 2½ years.

Stage 3: Advanced primary disease with inoperable regional glands.

Total 25: A/W 3 (5, 4, 4 years). Dead 22 (average survival 1·9 years).

One patient in this group who had radical mastectomy three months after therapy (and in whom the disease became operable without evidence of metastases) died of extensive generalized metastases within four months of operation.

If these three groups are combined:

Stages 1, 2, and 3: Alive 9 (7 over 5 years. All over 3 years.)

Dead 28.

Stage 4: Distant metastases.

Total 13 patients: All are dead.

1st year 9.

2nd year 3.

One survived for 6 years.

Recurrent disease.—Total 6 patients.

1 A/W 3 years.

Dead 5.

Carcinoma of the Tongue (including vallecula).

Total number 14. Alive 0. Dead 14.

Survival Dead

5—1st year 9 (1 untraced).

2—2nd year 3 (1 o.c. with healed primary and no glands).

1—3rd year 1

0—4th year 1 (died o.c. without recurrence of primary or glands).

(O.C. = other causes)

These were patients with advanced primary disease, together with glandular metastases, unilateral and fixed, or bilateral. In 6 patients the primary growth

regressed, without recurrence before the patient died from metastases. In 2 patients death was due to exhaustion and pulmonary metastases. In 8 patients, although some initial response was obtained in large glandular metastases, they rapidly recurred and extended. Mucosal reactions are severe with supervoltage, due to the large depth dose which can be delivered for a safe skin reaction. In spite of this, no difference was noted between those treated by million-volt therapy and deep X-ray therapy. Technically, however, it is easier to deliver the dose by million-volt therapy as an even distribution can be achieved by means of two opposing and parallel fields.

Carcinoma of the Antrum (1939-1945).

Total number of cases 20. Primary 13. Recurrent (following other forms of treatment) 7. All the cases with recurrent disease died within twelve months of treatment.

Survival (13 cases)

Alive 4.	8 years—1	Dead 9.	1st year 3 (1 senile decay. N.S.D.)
	5 years—1		2nd year 2
	3 years—2		3rd year 2
			4th year 1 50 months
			5th year 1 69 months
} Of disease			

(N.S.D. = No sign of disease—for which original treatment given)

All patients had advanced primary disease.

The average dose has been 4,500 r in twenty-one days through two oblique and opposed fields. The eye was included in an irradiated field in most patients and three out of four survivors have eye damage in the form of a radiation cataract. One of these has also a troublesome conjunctivitis and iritis, but apart from dimness of vision the other two are free of symptoms. Primary reactions are severe, but ultimate healing is good. The antrum has been explored in all, following therapy. Afterwards, all seem to have experienced some pain whilst dead bone was separating, but once this happened, pain was relieved, and with the fitting of an obturator they have been quite comfortable. The results are an improvement on ordinary deep X-ray therapy alone.

Extrinsic Carcinoma of the Larynx

This group includes growths of the pyriform fossa, aryepiglottic fold, epiglottis and pharyngeal wall. In two the primary was so large that the origin could not be determined.

Total cases 34. Males 29. Females 5. Two discarded, moribund on admission.

Stage 1: Local growth. 7 patients. 1 untraced.

Alive 1.	5 years.	Dead 5.	1st year 2
			2nd year 0
			3rd year 3

Stage 2: Mobile unilateral glands 7.

Alive 2.	1 at 5 years.	1 at 4 years.	Dead 5.	1st year 3
				2nd year 1
				3rd year 1
				} average 11 months.

Stage 3: Advanced primary with or without fixed glands.

Total 20 (Two moribund on admission).

All dead. Average survival 11 months.

Longest survival 3 years.

Absolute survival 3/32.

All the patients who died, died of their disease. In a few, large fixed masses became impalpable but they soon recurred, within the treated area. Of the three survivors, one had a carcinoma of the pyriform fossa with direct infiltration of the neck at the level of the primary. He is well with a strong voice, with slight persistent oedema following a tumour dose of only 3,000 r in fourteen days. In a second, the primary tumour was so large the origin could not be determined until it regressed. It was then thought to arise from the epiglottis. He also had hard mobile glands in the neck.

Intrinsic Carcinoma of the Larynx

Total 24.

Stage 1: A limited growth on a mobile cord. 1 case. Died 3rd year (senility also).

Stage 2: Whole cord involved or a fixed cord. 10 cases.

Alive 5.	3 at 5 years.	Dead 5.	1 o.c. and old age 18 months.
	2 at 4 years.		3 in 1st year.
			1 in 3rd year.

Stage 3: Both cords involved, or glandular metastases. 9 cases.

Alive 5.	1 at 5 years.	Dead 4.	3 in 1st year.
	2 at 4½ years.		1 o.c. in 2nd year.
	1 at 3½ years.		
	1 at 3 years.		

Recurrent: 4 cases. 3 dead.

2 in 1st year. 1 in 2nd year. 1 alive 5 years.

Summary: Total 20 cases.

Alive 10. 4 at 5 years. 4 at 4 years. 2 at 3 years.

Dead 10. Of disease 5. Of other causes, without evidence of laryngeal disease 2. Of damage due to treatment 3.

The recurrent cases were following fenestration and radium or surgical removal. Some palliation was achieved, but these died of disease; in one case growth was spreading and fungating in the irradiated area. One case survives five years:

Male, 56. 1941. Laryngo-fissure removal of left and anterior part right cord. 6/12 later hemilaryngectomy for recurrence. 2/12 later, post-operative deep X-ray therapy, 3,500 r in seventeen days. One year later, 1943, subglottic recurrence treated on million volt, 4,000 r in nineteen days. Remains well and free of recurrence to date (five years).

Most were treated through two opposing fields, either anteroposterior or lateral, the inequalities of the neck being filled up with bolus. "Dose" varied from 3,000 r in fourteen days to 6,000 r in thirty days. One patient with a well-differentiated squamous-cell carcinoma involving the whole of one fixed cord, and a hard lymph node in the neck, is alive and well five years after treatment, 3,000 r having been delivered to the tumour in ten days. Another patient, treated up to 4,500 r in twenty-seven days, developed a recurrence in the third year, on the cord. He had a laryngectomy, section of the cord being positive for carcinoma. Two cases in Stage 2 died from undoubted other causes (both were old and feeble) without any laryngeal symptoms. Another developed a local recurrence on the cord, four years after a dose of 5,600 r in twenty-eight days, delivered to the cord. He had so much fibrosis œdema and skin changes that further treatment was not possible, either surgery or radiotherapy.

Three other patients died from perichondritis and œdema within a few weeks of tracheotomy.

On the assets side, however, in 5 of the patients an absolutely fixed cord became mobile, and these survive.

Carcinoma of the Œsophagus(1) *Post-cricoid carcinoma*—

Total 15. Females 13. Males 2. With Plummer-Vinson syndrome 3 females. Alive 1. Dead 14.

The patient who survived had an early squamous-cell carcinoma in the post-cricoid region. 5,000 r was delivered in forty-six days, and apart from telangiectasia of skin and laryngeal mucosa she remains well, swallowing normally four years later.

Analysis of patients who died

At months	Alive	Dead	At months	Alive	Dead
6	11	3	24	5	0
12	7	4	30	3	2
18	5	2	36	2	1
			48	0	2

In all these dysphagia was relieved for varying periods of time, but later returned. Tumour dose varied from 4,500 r in sixteen days to 6,000 r in thirty-five days with an average of 5,000 r in twenty-eight days. 5 patients developed a local recurrence in the post-cricoid region, after doses of 4,500 to 5,000 r. All developed lymph-node metastases and 3 died from disseminated neoplasm. 4 patients had to have tracheotomy because of laryngeal obstruction due to œdema, and 2 of these, gastrostomy as well. The doses of radiation delivered are probably the maximum the tissues in this region can tolerate in this period of time.

(2) Carcinoma of the œsophagus proper—

Total treated 42. Males 33. Females 9. Youngest 37 years. Oldest 80 years. Average age 61 years. Alive 0. Dead 42.

At months	Alive	Dead
6	18	24
12	7	11
18	3	4
24	1	2
30	0	1

The average tumour dose has been 5,000 r in thirty days, delivered through six strip fields. Those patients treated up to 6,000 r in thirty-six to forty days did no better than those where only 4,000 r was given in twenty-eight days. In most patients dysphagia was relieved until the death of the patient. Apart from metastases, other causes of death were perforation of the œsophagus into the mediastinum, great vessels or lung. Some died suddenly of heart failure, and at post-mortem growth was found invading the heart muscle. 5 patients died suddenly following a sudden severe hæmorrhage, and in one of these at post-mortem there was no sign of growth, but the aorta and œsophagus communicated through a large smooth opening. There was no mediastinitis and no sign of X-ray necrosis above and below the aortic perforation. This particular case received a dose of 5,500 r in thirty-five days, and Phillips suggested that in these the appearances point to a failure on the part of the normal tissues to repair the gap left by the destruction of the carcinoma, so that the question of cure in carcinoma of the œsophagus appears to be less one of radiation dosage, than of tissue healing under adverse conditions. However, in at least 5 patients local recurrence of growth developed at the primary site, in 2 within six months, in 2 within twelve months and in 1 twenty-four months after treatment.

In 2 patients who died and on whom a post-mortem was performed, the pathologist was unable to find evidence of carcinoma. One death was from a perforation into the aorta and one from pneumonia.

Six patients died with extensive metastases in chest, liver, abdomen and spine.

Carcinoma of the Bronchus

Total cases 148. Palliative therapy for pain 46. Cases analysed 102. Males 94. Females 8. Average age 50 years. Youngest 20 years. Oldest 69 years.

Alive 2 (5 years, 4 years). Dead 100.

Died in months	Cases	Died in months	Cases
6	42	30	6
12	23	36	4
18	12	42	2
24	10	48	1
		60	0

} (90%)

Of the 2 patients who are alive:

(1) Woman, 46. 1943: Left pneumonectomy. The growth, a squamous-cell carcinoma, involved left pulmonary vein, and stump of this was left behind, together with growth on the pericardium. Well and active five years.

(2) Man, 57. Alive four years, free of clinical evidence of carcinoma. He has extensive pulmonary fibrosis, with a flat chest and scoliosis, the heart is drawn over. He has a cough, purulent sputum, some pain and marked dyspœa.

Intrinsic Carcinoma of the Larynx

Total 24.

Stage 1: A limited growth on a mobile cord. 1 case. Died 3rd year (senility also).*Stage 2:* Whole cord involved or a fixed cord. 10 cases.

Alive 5.	3 at 5 years.	Dead 5.	1 o.c. and old age 18 months.
	2 at 4 years.		3 in 1st year.
			1 in 3rd year.

Stage 3: Both cords involved, or glandular metastases. 9 cases.

Alive 5.	1 at 5 years.	Dead 4.	3 in 1st year.
	2 at 4½ years.		1 o.c. in 2nd year.
	1 at 3½ years.		
	1 at 3 years.		

Recurrent: 4 cases. 3 dead.

2 in 1st year. 1 in 2nd year. 1 alive 5 years.

Summary: Total 20 cases.

Alive 10. 4 at 5 years. 4 at 4 years. 2 at 3 years.

Dead 10. Of disease 5. Of other causes, without evidence of laryngeal disease 2. Of damage due to treatment 3.

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6	11	3	24	5	0
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18	5	2	36	2	1
			48	0	2

(1) *Recurrent disease*.—These patients had advanced disease, invading abdominal wall, rectum, &c. 4 died, the average survival being six and a half months. One is alive four and a half years after treatment:

Man, aged 70. 1936, partial cystectomy. 1941, recurrence—large sessile papilloma—fulgurated. Six months later, further recurrence. H.V. X-rays, 5,000 r in fifty-two days to the bladder. Two years later, 1943, further recurrence treated by H.V. X-rays to 5,000 r in forty-two days. He remains well to date (four and a half years).

(2) *Malignant ulceration with infiltrating carcinoma*.—All these 8 patients are dead, average survival being eight months. 2 patients died of other causes and at post-mortem no microscopic evidence of growth could be found. 2 further patients died from metastases with controlled primary disease. In 4 patients the primary growth was not affected.

(3) *Malignant papilloma*.—This forms the largest group, 7 out of 22 patients having survived for periods from two to five years. All had extensive bladder involvement—15 patients had had repeated fulgurations either cystoscopically or through open cystotomy for varying periods of time up to twelve years previously, the average being four years. 7 were new patients treated primarily by radiotherapy. 7 out of the 22 are alive and well, and 5 of these are nearing their fifth anniversary since treatment. They are symptom free.

Of those that died, 5 developed extensive papillomatous recurrences in the bladder following doses of 4,000 r and 5,000 r, one three months and one twenty months after treatment. In 2 of these there was no appreciable effect on the primary growths—but all had marked relief of hæmaturia.

In only one case is there evidence of severe damage to the bladder due to the treatment. One patient developed a desquamative cystitis following 4,500 r in six days which persisted and necessitated a total cystectomy. He died twenty months later from metastases.

Carcinoma of the Anal Canal

	Cases	Survived	Dead	Cases
Stage 1	3 (1 alive)	1	2 years	1st year .. 10
Stage 2	8 (3 alive)	4	3 years	2nd year .. 2
Stage 3	12 (4 alive)	2	5 years	3rd year .. 1
	—	1	6 years	4th year .. 1
Totals	23	8 alive	5 years	6th year .. 1 (o.c.)

Of the survivors, 3 had fixed inoperable lymph-node metastases in the groins, one had a large necrosis, another a small, dry, symptomless necrosis, whilst 2 have anal strictures, in both precluding the closure of a colostomy. One developed a local recurrence in the primary site and he had to have a perineo-abdominal excision.

Dead.—15 are dead, 10 dying in the first year after therapy. 12 were old and feeble, in poor general condition. In 7 the primary growth regressed completely and they died from metastases. One died five and a half years after treatment from a cerebral hæmorrhage, without local or metastatic disease.

Five patients had a serious radiation necrosis, probably responsible for the death of one. In only one of these did healing occur before death. One of these had further deep X-ray therapy at another hospital, whilst a second had radium applied. Both of these developed huge necroses.

Carcinoma of the Rectum

Total: 192 patients.

Stage 1	..	4	..	1 alive
Stage 2	..	18	..	1 alive
Stage 3	..	106	..	10 alive
Stage 4	..	12	..	0 alive
Recurrent	..	52	..	8 alive

192

20

Dead: 172.

The average tumour dose given has been 4,000 r in twenty-eight days, the maximum received being 5,000 r in fifty days.

Many cases were advanced when first seen and the general condition poor; they were ill patients, thin and wasted. Out of the 146, 59 had metastases when first seen, many had massive opacities and no attempt was made at selection. The length of history was short, the average being under six months, suggesting that carcinoma of the bronchus is a highly malignant cancer leading to cachexia sooner than most tumours. Although the oat-cell carcinoma appears the most sensitive type as judged by the radiological evidence of response, no marked prognostic difference was found between this growth and the squamous-cell variety. The average duration of symptoms in each was six months, and the average survival after treatment nine to nine and a half months. In carcinoma of the bronchus as it comes to us, 50% of treated patients are dead in six months, 75% in twelve months, and about 90 to 95% in two years. As Phillips noted, the problem is not entirely one of dosage, for cases treated to high dosage have done no better than those given a lower dose. Relief of symptoms is real, in most hæmoptysis will cease, and cough and dyspnœa are relieved, as a blocked bronchus reopens. In some, recurrence of growth occurred at the primary site, following heavy irradiation, and death was due to the effects of the primary tumour. Those patients who died within six months of treatment derived a little benefit, such as relief of hæmoptysis, or of spasms of dyspnœa. In very few was there no effect at all, but return of symptoms was rapid. In those that survived up to twelve to twenty-four months the initial response was greater, and some died of cerebral or bony metastases without return of chest symptoms, but in the large majority pain and cough returned, although hæmoptysis was controlled. One patient returned to heavy manual work for eighteen months. Of the 13 that survived over two years, 3 remained weak and poorly, but 10 regained almost normal health for twelve to twenty-four months, and then died from metastases with return of pains in the chest and cough.

Carcinoma of the Bladder

Total number of cases 40. 5 died within three weeks of admission. Cases analysed 35. Untraced 1. Males 25. Females 10. Alive 8. Dead 27.

Classification

(1) Recurrent disease after partial cystectomy.

Total 5.

Alive 1 (four and a half years).

Dead 4 (average survival six and a half months).

(2) Malignant ulceration.

Total 8.

Alive 0.

Dead 8. Average survival eight months. Longest twenty-six months. Shortest two months.

(3) Malignant papilloma.

Total 22. Males 15. Females 7.

Alive 7. 5 at 4—5 years.

2 at 2—3 years.

Dead 15. Average survival 13 months.

Group (a) Recurrence after repeated fulguration.

Total 15. Alive 5. Dead 10.

(b) Treated primarily by radiotherapy for extensive disease.

Total 7. Alive 2. Dead 5.

All Groups

	Dead	Survived
6 months	13	14
12 months	5	9
18 months	2	7
24 months	4	3
30 months	3	0

Million-Volt X-Ray Research at St. Bartholomew's Hospital

By N. S. FINZI, M.B., D.M.R.E.

THE objects of the research were to determine whether there were any advantage in the million-volt over the 200 kV machines already in use, either by increasing the proportion of successful results or by getting these results with less disturbance of the healthy tissues or the patients' general health. It was hoped to use the higher voltage under as nearly similar conditions to the 200 kV machines as was possible. This, however, was found to be impracticable as the weight of the applicators was so great that none but a very strong man could place them in the apparatus. The consequence was that the focal-skin distance had to be lengthened and a different method of localizing the rays by means of an adjustable diaphragm on the tube had to be employed. A lighting system was used to show the exact field on the patient. It was realized from the beginning that no staggering improvement in results was to be expected.

The research was planned on certain definite groups of cases, as already indicated by Dr. Williams. Unfortunately the war interfered very greatly with this programme. At the beginning, the department was shut completely for three months and, when it was reopened, it was found necessary owing to bombing to take cases outside the groups arranged, because on many occasions the 200 kV apparatus could not be used as it was on the fourth floor which had a glass roof. Alerts were frequent and bombs not unknown. Consequently there were many cases in which the machine had to be used for palliation only.

The results up to 1944 were published in Mr. Ralph Phillips' book: "Supervoltage X-ray Therapy", London.

Our treatment of breast carcinoma with the 200 kV apparatus does not equal the results of those treated at Manchester. I do not think this is due to any lack of skill in the application of these radiations, which were mostly in the very capable hands of Dr. Walter Levitt. They merely indicated a difference in the type of case with which the Department was supplied. For instance, stage 1 was almost unknown and stage 2 was relatively rare. The results in these breast cases treated in the million-volt department, therefore, must be compared with our 200 kV and not with those at Manchester. In the other groups our 200 kV figures are similar to Manchester's 250 kV. In many cases the figures are too small to be significant, but I think they are probably significant in the breast, the antrum, the intrinsic larynx, and possibly in the rectum cases. As regards these last, there is no question in the minds of those who have seen the cases that in many of them great palliation is obtained. For instance, a doctor came with an inoperable carcinoma of the rectum for which he had had a colostomy, but his pain was so intense that he felt something must be done. For a considerable time the pain was completely relieved, narcotics were stopped and he got back to his practice for over a year. He was known to have deposits in the liver before we started the treatment and this eventually caused a relatively peaceful and painless end. Palliation in many other cases was equally striking.

I can cite two cases in which the lower voltage had failed and the million-volt secured a successful result. One was a case of carcinoma of the body of the uterus in a very stout patient which I treated myself with 360 kV with rays having a H.V.L. in Cu of 3.9 mm. A local recurrence was treated a year and a half later with the same voltage, but there was a further recurrence in another eighteen months which was treated by the million-volt, and she has remained free from recurrence since that time for six and a half years, though she occasionally bleeds from telangiectases in the bladder. The other case is one of carcinoma of the vocal cords treated by laryngofissure in 1941. Recurrence six months later in the anterior commissure; treated

from the same source they are a fairly representative comparison of treatment in similar groups of patients.

Site	1,000 kV	200 kV (1925-38)	200 kV (1938-44)
Breast	25% (37)	9% (148)	—
Tongue	0% (14)	6% (109)	4% (45)
Antrum	30% (10)	12% (51)	—
Extrinsic larynx ..	10% (32)	5% (167)	7% (58)
Intrinsic larynx ..	50% (16)	22% (27)	15% (19)
Post-cricoid	7% (13)	0% (51)	—
Œsophagus	0% (42)	0% (143)	0% (71)
Bronchus	2% (102)	2% (145)	0% (58)
Bladder	32% (25)	—	—
Anal canal	29% (23)	—	—
Rectum	6% (98)	2% (43)	0% (6)

It can be seen that there is marked difference in results in breast, antrum, intrinsic larynx and rectum, a definite difference in extrinsic larynx, whilst in the bladder and anal canal, survivals have been obtained in sites previously not treated by X-ray therapy.

SUMMARY

In survivals no very marked difference or improvement can be shown, although I would like to emphasize that the cases treated seem to have been in very advanced stages of dissemination even for a radiotherapy department. Certain facts stand out:

(1) Those tumours that respond poorly to ordinary X-ray therapy show no very marked differences in response to million-volt therapy, with the possible exception of carcinoma of the rectum, carcinoma of the bladder, carcinoma of the antrum and carcinoma of the larynx.

(2) There is no evidence of any biological difference in response due to the shorter wavelength used.

(3) The question of dosage remains obscure. For instance, many tumours recurred in the treated area following heavy irradiation, others were arrested by 3,000 r in fourteen to twenty-one days.

(4) Any improvement in results is, I believe, due to the physical advantages of greater penetration, and greater accuracy due to ease of application, i.e. the treatment is more efficient.

(5) As Holmes and Leucutia have pointed out, "there is no quality dependence in that neoplasms that fail to respond to deep roentgen therapy can be destroyed by high voltage therapy".

It is a pleasure for me to acknowledge my debt and my gratitude:

For the foresight of Professor Hopwood, Dr. Finzi, Dr. Levitt, Dr. Donaldson and the late Dr. Canti and the Honorary Staff of St. Bartholomew's Hospital.

For the courage and hard work carried out under the trying circumstances of the war and his own ill-health of Mr. Ralph Phillips. These were mostly his patients, it is his labour, and I am but giving the results of his efforts.

For the toil, labour and perseverance of Mr. George S. Innes, who built, cared for and maintained the machine as well as being responsible for all the Physical work. My thanks are also due to Mrs. Yendall, Miss Brewer, and our Welfare Department.

" 'Tis weary watching wave by wave
And yet the tide heaves onward.
We climb, like coral, grave by grave
That pave a pathway sunward.
We're driven back, for our next fray
A newer strength to borrow,
And where the vanguard camps today
The rear shall rest tomorrow."

Section of Ophthalmology

President—HAROLD LEVY, F.R.C.S.

[February 13, 1948]

MEETING HELD AT THE BIRMINGHAM AND MIDLAND EYE HOSPITAL, BIRMINGHAM

Demonstration: Fundus Photography in Colour

Dr. H. Campbell Orr (Wolverhampton) gave a demonstration on this subject, illustrated by a large series of colour slides. With the history of the photography of the fundus, he said, they were all well acquainted, but of the practical difficulties many of those present probably knew nothing. Using the Zeiss-Nordensen reflex-free camera, he was formerly able to obtain colour photographs of the fundus with an exposure of about one-fifth of a second, but now, for some reason, the exposure had to be about half a second, which was something of a strain on the patient, with the result that too frequently there was a slight movement of the eye.

He showed first of all a view of the normal fundus, illustrating how sharp the focus could be and how clearly the detail could be seen. His next photograph was taken to show small white glistening dots in the macular area. He drew attention to the delineation of the column of blood in the upper vessel. The young man in whose macula these white spots were present went through the whole of the African campaign and had no difficulty at all. The next example was of the fundus in retinitis pigmentosa, illustrating the characteristic pigment changes. A striking case was one in which there had been avulsion of the optic nerve. The patient had a motor accident in which the optic nerve was pulled out of the back of his eye, "just like a cork out of a bottle", and the picture showed how the fibrous tissue had filled the gap. In another case, the fundus of which was shown, the patient had a history of a blow on the eye with a snowball some years before. A detachment had resulted which healed spontaneously. The photograph was taken about eight or nine years ago, and the latest information was that the patient had developed a cataract of this eye.

In showing a picture of a case of coloboma of the macula, Dr. Campbell Orr said that the case was specially interesting in that the grandmother, the mother, and the child all had the same condition. His next case showed the early stage of arteriosclerotic retinitis, with the sclerotic changes well in evidence. The next, with considerable retinal changes, was a man who had had Paget's disease twelve years earlier. One case, which had been thoroughly investigated, was one of what appeared to be albuminuric retinitis. He saw the patient first at hospital, and thought it an ordinary refraction case, and having made the examination, told her to come back the following week to be fitted with glasses. The patient, however, did not improve. Minute dots were noticed around the macula, which was photographed. The appearance became worse and was photographed at intervals of five weeks. But the interesting thing about the case was that no albumin was ever found in the urine, and there was nothing else to suggest a kidney lesion. On a later examination the whole condition appeared to have cleared up. The vision was now 6/12 without glasses and 6/9 with glasses, and only a few pigment changes remained.

The next case was of a boy with myopia who came to see him once a year to have his glasses corrected. On one of these occasions he found optic neuritis and queried cerebral tumour. The boy was sent to a specialist in Birmingham who investigated the case but could find nothing. He saw him again three months later and the appearance was practically the same as in the earlier photograph. This time he insisted that the boy should go to a neurologist, and he was proved to have cerebral tumour. He died the day after his operation.

Two pictures of the fundus in the same patient were next shown. This was a young woman who had been under treatment from Christmas 1939 until June 1940, when she was sent from Birmingham to Glasgow, and there an operation took place, a tumour the size of a small tangerine orange being removed from the base of the brain. She came back to Birmingham, and when he last saw her she was perfectly fit and well, with nothing to suggest any trouble except for a little white fluffy appearance on the disc which, if one did not know the history, one would not have put down as anything abnormal.

The next case was one of papilloedema. The patient had had a malignant growth removed from her breast. The fundus picture showed very marked pale swelling of the optic disc. She was returned to her own doctor and was followed up for six years afterwards, but no trace of secondary growth was discovered. Why she should have had this fundus appearance without showing definite evidence of secondary growth he did not know. The next was a case of disseminated sclerosis. He pointed out a shadow which interested him in the picture of the fundus. This was followed by a case of typical macular chorioretinitis. In diabetic patients a slight haze was seen in the fundus which made it extremely difficult to get a clear

200 kV, dose 3,450 r in fifteen days, second degree skin reaction. March 1943: Large subglottic recurrence, treated on million-volt, 4,000 r in nineteen days. Now, five years later, remains well. The dose, when the biological difference of the radiation and the time factor are taken into account, would be approximately the same.

The occurrence of necrosis was almost entirely in the early cases, when the treatment was being investigated, and when large fields were used. Later, multiple small fields, carefully checked by isodose charts in each case, were used and this has probably very much diminished these troubles.

When one gets used to the method of working, I should consider the million-volt more accurate, and, by using a suitable technique, one could get results with far less damage to normal tissues and also, as the volume dose proves to be smaller, with less disturbance of the patient's general health.

Apart altogether from improvement in results, one would feel that this apparatus is an advance, even if the statistics were no better than with the lower voltage. Those who have worked with it prefer it to the lower-voltage installations on account both of ease of manipulation and the greater accuracy that can be attained. Correct localization depends upon the radiotherapist's clinical knowledge and acumen and results will always to an extent be influenced by this.

Actually the improvement in certain cases is large enough to justify the hope that with further experience we shall get better results and, with a greater increase in voltage, one might get better results still. As it is, the results improve from year to year. One thing must be remembered: if one's successes with 200 kV amount in a particular type of case to 15% and with 1,000 kV to 20%, this increase, although only 5% on the total cases, is actually an increase of 33% of the previous successful results.

We consider, therefore, that a still higher voltage should be tried and some years ago a fund was started at St. Bartholomew's Hospital for this purpose and to this, Mrs. Sassoon has contributed liberally, and a patient of mine also contributed a considerable sum through myself. There is some difference of opinion as to whether we make a big jump up or whether we try the intermediate voltages. Personally, I am very strongly in favour of not too big a jump in case we should miss the optimum biological voltage. Also there is always the possibility of unexpected difficulties. We should aim at a machine which could work at first at from 3 to 5 million volts, but which could be subsequently put up to 20 million volts.

One question on which we had hoped to get information if we got improved results was whether there was any biological difference or whether it was only due to being able to get the radiation to the correct place in sufficient amount. It seems to me that the improvement in the results in the antrum and in the intrinsic larynx cases is strongly in favour of a biological difference, though in most of the other cases the improved results could be attributed to physical differences and in the skin to a chemical effect.

I suggest that the million-volt machine shows already a definite advance and indicates that malignant disease should be treated by higher voltages still.

I wish to record my most grateful thanks to all those who have worked and are working in this important research; particularly to Professor Hopwood, the late Dr. Canti, Dr. Donaldson, Dr. Levitt, Mr. Ralph Phillips, Dr. I. G. Williams, and to Mr. G. S. Innes.

Bilateral Facial Paralysis and Abducens Palsy (Two Cases).—A. A. DOUGLAS, F.R.C.S.Ed.

Jean W., aged 11, and John A., aged 6. The two children showed an almost identical degree of nuclear agenesis, which presumably led to the striking similarity—not only facial, but also of the tongue, palate, teeth and indeed of the body generally.

Jean was of the hypothalamic type and John was putting on weight. Both had complete bilateral facial paralysis and congenital abduction deficiency. Both had had difficulty in swallowing during their first two years and showed evidence of affection of the twelfth nerves.

By a strange coincidence, both had been brought to the Out-patient Department on the same afternoon.

The ocular movements showed many interesting features. Movements of dextro- or levo-version were absent and apart from head movements refixation could only be achieved by convergence, which was accompanied by contraction of the pupils, whether near or distant objects were fixed. Bell's phenomenon was well seen in both cases.

Presumably tracts in the region of the oculomotor nuclei were affected.

Bilateral Corneal Lesions Caused by Blast.—A. A. DOUGLAS, F.R.C.S.Ed.

This patient was an elderly man, who had been involved in a factory explosion. He sustained very little general injury, but a few hours later had photophobia and dimness of vision. When seen the following day, he presented a striking bilateral corneal lesion unfamiliar to the exhibitor.

There was oedema of the epithelium. From the centre of each cornea, doubly contoured grey lines radiated, which branched and enclosed between them polygonal areas milky white in appearance.

Slit-lamp examination showed that the doubly contoured lines were indentations of the posterior corneal surface and that the polygonal areas protruded into the anterior chamber, the whole cornea being very greatly thickened. This was Phase 1. A month later the condition had greatly changed.

Phase 2: The doubly contoured lines were now protruding more posteriorly; the polygonal areas were now only faintly opaque; the cornea was of normal thickness. The lines were now clearly seen to be folds in Descemet's membrane. When the beam fell on them at certain angles, they looked like streaks of viscous fluid on the posterior corneal surface. Vision (from less than 6/60 each eye) had now risen to 6/24 and 6/18. One month later the condition had reverted to Phase 1 and the vision had again deteriorated: it was at present again in Phase 2, but this time the vision had improved very little. It seemed likely that the appearances in Phase 1 were due to the entrance of fluid into the corneal substance, which became swollen and hydropic.

No alteration in the intra-ocular tension was observed.

Mr. P. Jameson Evans said that he had seen blast injuries arising from enemy action, though he had not followed these cases through. Similar conditions might arise after cataract extraction, where, even after a period of recovery of some six months, the cornea would be divided up into small polygonal areas. He had seen two such cataract cases, and apparently the condition became permanent.

Five cases by P. JAMESON EVANS, F.R.C.S.

Mr. Jameson Evans said that the first three of these cases were exhibited to show the effect of irradiation in regard to vasosclerosis.

I. Persistent Keratitis.

Male, aged 24.

This was a case of persistent keratitis of about two years' duration which had recovered and the patient had resumed an active life. When first seen, the condition looked strumous. It had been treated in various ways, including the use of tuberculin, but still persisted with active vascularity of the cornea in the interstitial layer. It was treated by stitching a 2 milli-curie radon seed underneath the conjunctiva close to the limbus and overlying the major vessels encroaching on the cornea; forty-eight hours later the seed was removed. Within twelve months the vision, which had been 6/60 or less, began to improve, and within eighteen months the vision was 6/12 and the opacity in the cornea had almost entirely absorbed.

II. Acne Rosacea Keratitis.

Male, aged 56.

The second case was similar to Case I—an acne rosacea keratitis which had resisted all sorts of treatment and was getting more and more frequently involved in attacks of vascularity. This was treated with two radon seeds on the nasal side under the conjunctiva, one in each eye, left in for forty-eight hours. It was noticeable that in this case there was very much less reaction to the radon, and the sclerosis of the vessels appeared to come on more quickly. That was about nine months ago, and there had been no recurrence of active vascularity of either eye since.

picture. Rarely did one get a picture of the diabetic fundus in which the detail was clearly seen, any more than in the view with the ophthalmoscope. But he pointed out how the changes in the vessel wall were gradually thinning down the stream of blood. In the case exhibited the blood-pressure was 220, and the albumin was rather marked in the urine, but the patient lived for at least three years after the picture was taken. The next example showed symmetrical macular degeneration in an old man with arteriosclerosis.

A great deal of information was obtainable from the appearance of the venous system of the fundus in such cases as diabetic retinitis. In some cases it was interesting to use the Gullstrand ophthalmoscope, with which the corpuscles could be seen rolling over and over in their passage down the vessel, the blood-stream having been slowed very considerably.

Dr. Campbell Orr showed the views of several other fundi, including one in the case of a stout plethoric individual, with a blood-pressure of 210, and another in an old lady of 70, with a blood-pressure of 240 and senile macular changes.

The fundus was shown of one interesting case in which a piece of steel had been embedded in the eye. The patient had felt a blow on the eye but had not paid much attention to it until he noticed, some time later, that he could not see quite as well as formerly. He came to hospital where the photograph of the fundus showed the piece of steel and how the fibrous tissue from the wound of entry above came down and covered the foreign body. Yet that piece of steel had not been in the eye for more than a few days. He always held that with a metallic foreign body which was magnetic the magnet should be applied first and the X-rays afterwards. Every hour that was lost made it more difficult to get the foreign body out. The X-ray photograph could be used afterwards if the magnet had failed. The rapidity with which this piece of steel was sheathed by the fibrous tissue was instructive.

The next patient whose fundus was shown was aged 72 and had detachment of the retina. Deutschmann's operation was done in 1922, and afterwards no view of the fundus could be obtained for many years. A picture of the eye of the same patient was taken recently because of the choroidal sclerosis. The retina was right back in position, but the eye was blind. The lecturer's final picture showed a case of choroideremia.

Three cases by Mrs. D. R. CAMPBELL, M.B.

I. Bitot Spot (photograph and report).

The interest of this case lies in the association of Bitot spot with a particularly low blood vitamin A. The patient had a Bitot spot of some size, and for about three months previously he had been on big doses of vitamin A. After these were stopped his blood vitamin A fell from 192 International Units per 100 ml. to 39 on one occasion, and 46 on another. In comparison a large number of estimations had been carried out at the hospital on normal individuals following various occupations, for about a year, and on present rationing the vitamin content of the blood was level—about 100.

The conjunctivæ in this patient were opaque and yellow, and the whole face was lustreless. On vitamin A his complexion improved, and the conjunctivæ regained a pink colour, but the Bitot spot did not disappear. It was possible to scrape off foamy epithelium, leaving a crater. It was subsequently excised, and the patient had had no recurrence.

Discussion.—A member asked what was the nationality of this patient and was informed that he was English. He said that he had seen Bitot spot in Arabs.

II. Bilateral Microphthalmos with Orbital Cyst.

This girl, who had been born blind, did not come to hospital until she was 18, when the cysts had become swollen, and one in the right eye, in the lower lid, was distended and was causing pain. The cysts were taken out, and with the idea of keeping the conjunctiva as far as possible, an external canthorhaphy was done, the lid margin was split, the cyst was dissected from below, and then everted right out. A good layer of conjunctiva remained, with a central hole, corresponding to the limbal margin of a normal eye. The patient was fitted with a pair of small artificial eyes which gave her a rather more normal appearance.

Primitive retinal tissue and the optic nerve were visible in the right cyst. The specimen from the left side showed a rudimentary eye with primitive cornea, pigmented uveal tissue, and a mass of tissue which corresponded to the lens. Posteriorly there was a patch of primitive neural tissue and another outside the rudimentary eye.

III. Sjögren's Disease: Case fitted with Contact Lenses.

All the symptoms and signs of Sjögren's disease were present in this case—parotid swelling and keratitis, &c. The patient also had rheumatic signs and still had intermittent pyrexia. She had had X-ray therapy to the parotids. The case had been diagnosed but no one could produce any better treatment for her. Cauterization of the punctæ brought about temporary improvement. Finally she had contact lenses, and was very much better so far as the eyes were concerned, but her general health was deteriorating. Vitamin therapy of all kinds had been tried, including riboflavine. The blood vitamin A was estimated and was perfectly normal.

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Mr. Jameson Evans hoped to be able to show the case again in twelve months' time and to report that she had not had a recurrence of hæmorrhage.

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Female, aged 18.

The patient had a typical subluxation of the lenses. She had long fingers and limbs, was very tall, and had a heart murmur.

V. Temple-Smith Operation.

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This case was shown to illustrate the result of the Temple-Smith or Himmelsheim operation, which had taken place about fifteen months previously. The child had an external rectus palsy of the left eye, and was treated by double tendon slip graft. In this case it was combined with a recession of the internal rectus. Her internal movement was not quite full.

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Mr. Galloway said that this case showed a condition not often described and one, he thought, of great interest. The child was a twin and nine weeks premature. There was microphthalmia and nystagmus. The pupils did not react to light when he first saw them, and he could not make out whether the child could see or not. There was no history of similar trouble in the family. Terry had published very similar cases in *Archives of Ophthalmology*, Chicago, 1943, 29, 36.

In the discussion in the *Archives* there seemed to be a good deal of difference of opinion as to methods of treatment. In some of the cases the fibrous mass at the back of the lens had ruptured spontaneously after some months, allowing the fundus to be seen.

Mr. A. S. Philips said that in Mr. Galloway's case of persistence of the posterior vascular sheath of the lens he would needle the lens first, and when the lens substance had absorbed he would divide the tissue at the back with a Wheeler's knife.

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Mr. I. Lloyd Johnstone said that he had had some experience of cataract and microphthalmia with mental abnormality in young children. He thought there was a definite syndrome. He had tried to trace any relationship with illness during the mother's pregnancy, but had not succeeded. Some of these children had been under observation for seven years, and it was difficult to say how much they could see.

Meningioma en Plaque of Inner Sphenoidal Ridge (Two Cases).—BRODIE HUGHES, F.R.C.S.

CASE I. Mrs. A. K., aged 47. (Referred by Mr. G. N. Pattison.)

Localized left frontal headaches of five years' duration—failing vision left eye for three months. Vision and field of right eye normal, and no abnormality in the nervous system apart from left eye.

Left eye displaced forward, but no limitation of external ocular movement. No pulsation and no tumour palpable in the orbit. Vision reduced to doubtful light perception at the field periphery. Fundus: severe primary optic atrophy. X-rays show diffuse hyperostosis with bone sclerosis affecting the inner sphenoidal ridge and roof of orbit on the left side. Optic canal is narrowed and its whole circumference affected by the bony lesion.

Operation on 20.10.47: Small left frontal bone flap—no intradural tumour found but dura over affected bone was thickened and hyperæmic. Posterior half of orbital roof and

whole of sphenoidal ridge removed together with the superior and lateral walls of optic canal.

No recovery of vision but some diminution in proptosis.

CASE II. Mrs. E. G., aged 43. (Referred by Mr. C. Rudd.)

Localized right frontal headache for three years—failing vision and protrusion of the right eye for six months.

Abnormal physical signs confined to the right eye. This is displaced forwards but without limitation of external ocular movement. Vision reduced to bare light perception—fundus shows severe primary optic atrophy.

X-rays showed localized hyperostosis of the inner third of the sphenoidal ridge surrounding the optic canal.

Operation on 7.11.47: Small right frontal bone flap and removal of the whole of the sphenoidal ridge together with the superior and lateral walls of the optic canal.

No recovery of vision but some decrease in proptosis.

Monocular Congenital Cataract.—I. LLOYD JOHNSTONE, M.C., M.D.

Mr. Lloyd Johnstone said that the main points of the case were that it was monocular and had an interesting and unusual slit-lamp appearance: (a) slight anterior opacity; (b) perinuclear fine granular spotting; (c) posterior white fluffy ring with a hole in the centre.

Chainmaker's Cataract.—L. H. G. MOORE, M.B., Ch.B., D.O.M.S.

Dr. Moore said that in the Black Country chains were still made by hand and the workers developed this particular type of cataract. The case presented showed well the exfoliation of the anterior capsule. The ordinary link-maker worked always with the fire on his left, and his left cataract was always to a certain extent in advance of his right. It was because of the exfoliation of the lamella of the anterior capsule that he had brought this patient along.

In reply to the President, who asked whether it was possible to get these people to wear protective goggles, Dr. Moore said that they would not wear anything which they were compelled frequently to take off and wipe.

Mr. Lloyd Johnstone said that the condition took about twenty-five years to develop and that the workers could not see the reason for wearing protective goggles because of this long period.

Melanotic Sarcoma of Choroid in Second Eye, treated by Radon.—C. RUDD, M.B.

Mr. Rudd said this was an interesting case because the patient had had the left eye removed for definite sarcoma of the choroid in 1942, and two years later came up with a perfectly typical melanotic sarcoma in the other eye. He was reluctant to excise the second eye and so he had tried radon. The marked atrophy of the choroid in the region of the mass could be observed and the growth was smaller than formerly. The vision was 6/24.

Tumour of the Para-macular Region.—Major K. MEHTA, M.B. (introduced by P. JAMESON EVANS, F.R.C.S.).

Mr. Jameson Evans said that this was the case of a soldier with a raised mass below and extending out from the left macula. The mass showed pigmentary changes at the edges. The history was of three years' duration, and there had been no improvement of vision.

The general consensus of opinion among members was that the condition was exudative and allied to Coats's disease.

Angioma of Retina.—FLORENCE HENRY, M.B. (introduced by C. RUDD, M.B.).

Mr. Rudd, on behalf of Dr. Henry, said that this was the case of a child with a whitish patch in the retina. It has been observed now for about five years and there had been no change.

The following cases were also shown:

(1) Opaque Nerve Fibres. (2) Von Hippel's Disease.—Mr. H. W. ARCHER-HALL.

Foreign Body in Upper Temporal Quadrant.—Dr. H. CAMPBELL ORR.

Central Exudative Retinitis.—Mr. P. JAMESON EVANS.

Macular Swelling (for Diagnosis).—Mr. N. P. R. GALLOWAY.

Retinal Hole.—Mr. I. LLOYD JOHNSTONE.

Foreign Body on Iris, Simulating Neoplasm.—Mr. T. P. KERWICK.

(1) Exudative Retinitis. ? Coats's Disease. (2) Congenital Absence of Orbicularis Oculi.—Mr. C. MARTIN-DOYLE.

(1) Sjögren's Disease. (2) Central Retinopathy.—? Exudative, ? Neoplastic—for Diagnosis.—Mr. C. RUDD.

Arteriovenous Fistula at Base of Skull.—Mr. R. W. STEPHENSON.

Patch in Lower Part of Lens.—Mr. J. G. DRUMMOND CURRIE.

OCT.—OPHTHAL. 2.

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discs were of good colour and the vessels of the retina of good size. The question arose whether it was a congenital condition or an inflammatory condition of some sort. There was no opacity in the vitreous and with such a degree of inflammatory lesion one might have

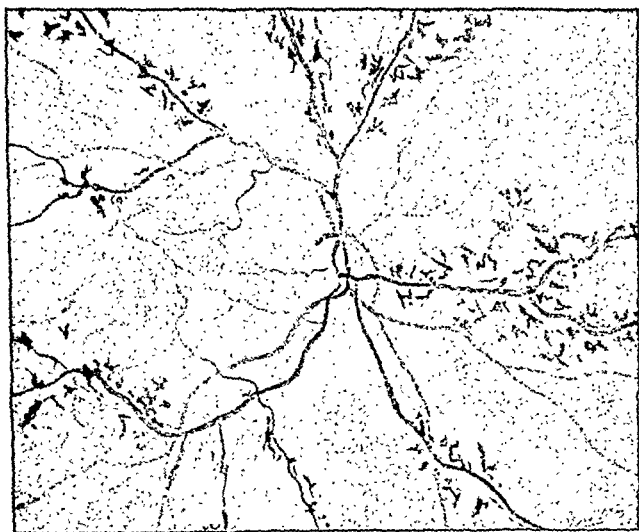


FIG. 1.

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Mr. Frank Law said that he had notes of a similar case. This was in a lady, aged 37, who was sent to him in 1943 because she was worried about her eyes. She said that her vision had always been bad. Her vision corrected was 6/12 in the right eye and a little over 6/18 in the left. He found similar changes in both fundi limited to the distribution of the vessels, in particular the veins. The pigment was coarse. The vessels were rather small and the discs yellowish in colour. The choroid was well seen in the areas concerned. He had never seen anything like it before. The patient had told him she was very fair as a child. She had married at the age of 22, and she had one child. The Wassermann was negative.

The appearance of the fields and the vision were unchanged in 1946 and in 1947. When she came to see him in 1946 she was pregnant and he wondered what the effect of the nervous and emotional strain associated with pregnancy would be upon her eye condition, but she miscarried at 3 months.

He showed a drawing of the appearance of the fundus. The colour of the disc was rather meagre, but the choroid, in particular in one area on the inferior part, was seen very clearly. It was not quite so well marked along the course of each vessel as in Mr. Morgan's case. The fields (which he showed) were extremely difficult to take.

Hypertensive Retinal Changes and Sympathectomy.—R. W. STEPHENSON, D.O.M.S.

J. S., male, 38.

April 28, 1947: Five years ago began to have severe headaches. His doctor found high blood-pressure. Condition improved with conservative measures. Recurrence of symptoms two years later, similarly relieved. A week ago R. vision misty, rapidly getting worse and affecting nasal side of field. V.R. 6/12 part.; V.L. 6/5. R. fundus: Some swelling of disc. Haemorrhages and exudates especially in lower temporal quadrant. Marked arteriosclerotic changes. Veins very tortuous and somewhat engorged, arteries narrowed. L. fundus: Similar to right but changes less marked. R. field contracted to within a few degrees of fixation point on nasal side, full on lower temporal side.

I advised that he was probably a suitable case for sympathectomy, as this would offer the only chance of ameliorating his condition and prolonging his life.

He was sent to Mr. A. L. d'Abreu of Birmingham.

C.N.S.: Pulse regular, 84. B.P. 220/150 remaining very constant during preliminary rest period. X-ray of chest showed increase in cardiac diameter.

[March 11, 1948]

? Conglomerate Tubercle. ? Sarcoidosis of the Iris.—A. J. CAMERON, F.R.C.S.

F. O'C., married woman, aged 25.

History.—This case was seen on routine "Out-Patient" examination on 3.11.47 when a history was given that her baby had poked a finger in the left eye. Previous history: "nervous breakdown" following upon childbirth in April to November 1946, and erythema nodosum in November 1947.

On examination.—There were massive "K.P." all over the cornea and a mass in the angle of the anterior chamber.

A diagnosis was made of ? Conglomerate Tubercle.

Investigations.—Kahn test negative. Mantoux test negative.

Blood-count.—Hb 96%; R.B.C. 5,000,000; C.I. 0.96; mean diameter 7.15μ ; W.B.C. 6,400 (polys. 59%, eosinos. 4%, basos. 1%, monos. 9%, lymphos. 27%). E.S.R. 14 mm. in 1 hour.

X-ray report: "Fairly extensive interstitial fibrosis and increased vascular markings of both lungs. Enlarged hilar shadows. The appearances are those of a Boeck's sarcoidosis."

Further X-rays revealed no other abnormality.

Dr. Clifford Hoyle of the Brompton Hospital reported: "The clinical course is that of sarcoid in its strikingly benign character with so little disturbance of her general health and so little in the way of focal symptoms, in spite of extensive lesions in both lungs and the bronchopulmonary glands. Moreover, the lesions are not changing rapidly radiologically, nor showing progressive cavitation. But, on the other hand, we not uncommonly see all these features early on in cases that later prove, by a positive sputum or biopsy findings, to have been tuberculous all along."

7.2.48: A new and separate nodule was found deep in the anterior chamber, about five o'clock, and the previous generalized mass seemed, perhaps, a little less.

25.2.48: The original mass had receded considerably and could just be seen deep in the angle with a large adhesion of the iris just about six o'clock on the margin of the pupil and a secondary nodule adjacent to it.

It is interesting that the condition remained stationary and quiescent for so long and then suddenly began to regress, but according to Parsons and to Duke-Elder that is, of course, the usual procedure which a conglomerate tubercle follows. It is also of some interest that the radiologist should have diagnosed sarcoid disease from the X-rays alone.

The patient's general appearance is good and she has been treated simply locally with atropine and her general health improved as far as possible.

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I. Corneal Graft of Thirteen Years' Duration.

This patient had a 4 mm. circular corneal graft carried out in December 1934. Her vision is now 6/36 and she is able to get about by herself and do her own shopping and housework (see *Brit. med. J.*, 1935 (i), 919). She has been removed from the Blind Register.

Mr. Rycroft, in reply to a question by Mr. E. F. King, said that he had used a 4.1 mm. trephine and had trimmed the edge with scissors and forceps all the way round.

II. Malignant Hypertension with Severe Retinopathy, treated by Lumbothoracic Sympathectomy.

This patient was seen in July 1946 with severe papilloedema and superficial retinal haemorrhages of both eyes. In September 1946 Mr. R. C. Brock carried out lumbothoracic sympathectomy and there has been a steady improvement ever since then. Present condition: R.V. 6/9—L.V. 6/5.

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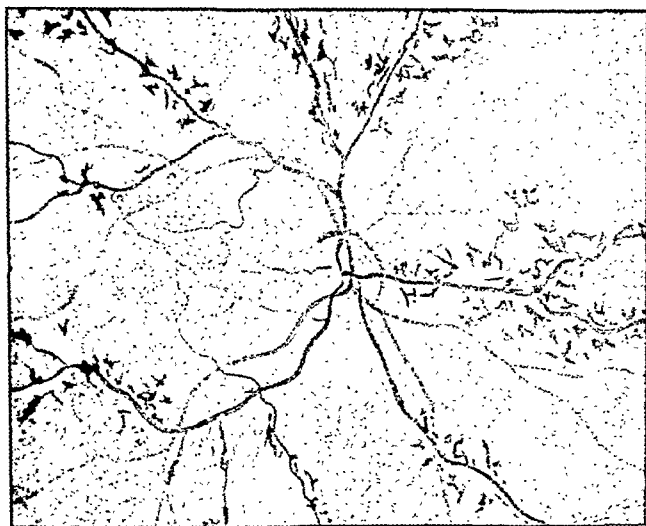


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perfectly normal raised blood-pressure. As a result of emotion, as we saw frequently in young recruits, such an individual may have a systolic pressure sent up to 160 or 180 with some increase in the diastolic. This is transient and then, as years go by, occur these changes in the kidney to which I have referred, the formation of the renal by-pass with a more persistent renin formation, and simultaneously the slowly increasing blood-pressure. Still at this stage there is the added effect of emotion, so that there is transitory spasm in the healthy parts of these kidneys, and therefore we have not only the permanent part of hypertension but also the transitory part as well.

It is not until perhaps the age of 40 or even higher that the arteriosclerotic degeneration occurs. This, of course, takes place in all sorts of diseases, but it seems to affect the kidney before anything else. It may also involve the coronary circulation, and it may and frequently does affect the retina as well. The heart remains normal and, unless there is arteriosclerosis of the coronary circulation or of the cerebral circulation, the individual will not have a vascular lesion.

I think it is perhaps true to say that hypertension itself is harmless. That sounds paradoxical. But we have all of us seen people in whom at the age of 20 a somewhat raised blood-pressure is found, and who for twenty years have remained perfectly well, without symptoms and without any change. I asked the Swedish surgeons who have been interested in coarctation of the aorta whether, in their cases, they had ever met retinitis as a result of what amounts to experimental hypertension in healthy young adults. They had never met it, so that it would seem that hypertension does not produce retinitis or other changes alone provided the blood-vessels remain healthy. In these cases one has a very good control experiment.

The cause of the hypertensive vascular complications is—to use the old phrase perhaps advisedly—a softening of the arteries. The change that occurs in every aorta at the age of 40-60 is atheroma. There are degenerative changes in the smaller vessels also but this is a separate change, it is a degeneration quite apart from that caused by hypertension. The change may be sometimes exaggerated and brought forward in the terms of the patient's age. For example, in a young individual with nephritis, whether it be due to a positive poisoning or to some negative deficiency, the arterial system shows this degeneration to a very extensive degree and very early, and I think it is extremely important to bring this point before ophthalmologists, because it means that in the search for a further explanation one must not be satisfied with hypertension alone as being the cause of retinitis in hypertension.

I have the notes of the case of such a young man, aged 21, who had what was called malignant hypertension. As a result of sympathectomy (this was the second operation) his systolic pressure fell from 220 to about 160 and his diastolic from 140 to about 120. He had a transitory increase in the blood urea which was afterwards considerably improved. The interesting thing is that sympathectomy in this sort of case clears up to an amazing extent the retinopathy, but it does not permanently cure the patient of the hypertension. I have at the present moment in my wards one of these patients who was very nearly blind and had extensive changes in his retinae which were cleared up so that he can now read small print whereas previously he could not read large headlines. But he has now again been admitted, this time with severe hypertension and heart failure. His blood-pressure is quite as high as before but his retinae have remained normal, so it would seem that the improvement of his renal circulation has helped in the regression of the degenerative process in the retinae. It has not permanently affected the hypertension, however, and one would not expect it to do so, because he must have permanently diseased kidneys from which renin is still coming.

When is sympathectomy justifiable? It may on the one hand be done twenty years before it is necessary. But on the other hand if it is done too late there is an established and permanent degeneration in the kidneys. Therefore one has to remember (1) that the changes in the kidney are usually in advance of those which occur in the retina, and (2) that it is upon the ophthalmic surgeon that we very greatly rely in helping us to decide what is the state of the visible peripheral arteries. It seems to me that certain definite criteria should be fixed to try to determine when the arteries in the kidney are perfectly normal, when there is spasm only, and when there is sclerosis; also, of course, the final change when there is papilloedema and hæmorrhage.

For research in the young adult records might be taken of specific vessels in the same patient from time to time and the effect of amyl nitrite or sodium amytal, which causes relaxation of the arterial pressure, might be elicited. Simultaneously a photographic examination might be made of the retina. It might be possible, on these lines, to produce and make available a series of tests that will tell us exactly what the retinal arteries are doing in the earlier stages.

Mr. E. G. Tuckwell: Sympathectomy and splanchnic neurectomy are often unsuccessful in lowering the blood-pressure to a normal figure, but it is apparent that the symptoms of the patient are relieved in a great many more cases; I believe this to be due to the fact that after operation the blood-pressure is steadier at a mean level, and that the fluctuating pressure

Renal functions: Blood urea 48 mg.%; urea concentration test—to 3.2%; urea clearance: 1st hour 131% of normal; 2nd hour 178% of normal. Urine: occasional hyaline and granular casts, otherwise normal.

Bilateral two-stage transthoraco-lumbar sympathectomy on 13.5.47 and 3.6.47.

Symptomatic improvement with freedom from headache. B.P. 185/140.

August 2, 1947: B.P. 185/100. V.R. 6/6 pt. V.L. 6/5. Fundi: No hæmorrhages or exudates or œdema. October 1947: B.P. 178/120; November and December: 180/120. January 180/125.

March 3, 1948: V.R. 6/6 with +0.5 D.sph. = 6/5 pt. V.L. 6/5 pt. with +0.5 D.sph. = 6/5.

R. fundus: No hæmorrhages or exudates. Arteries show very marked narrowing and sheathing. The veins are normal in calibre.

L. fundus: Similar to above but narrowing and sheathing not so marked as in R.

R. field still shows contraction on nasal side.

The most interesting point in the case is the considerable increase in the arteriosclerotic changes in the retinal vessels since the operation.

DISCUSSION ON THE EFFECT OF SYMPATHECTOMY ON HYPERTENSIVE RETINAL CHANGES

Dr. Geoffrey Bourne: It was thought for many years that raised blood-pressure was due to an actual sclerosis of the peripheral circulation. This, we know now, is not the case. The actual hypertension itself is, from the first to the last, spasmodic in its nature. It probably starts in the 'teens in many cases and it is then very little more than an excessive physiological reaction.

It is thought now by Trueta that the actual pressor substances formed by the kidney may at first be, as it were, a physiological reaction, and he tentatively suggests that in certain individuals psychological stimuli—the ordinary stimuli of the emotions, fear or excitement—do actually produce a blanching of the renal cortex. From this blanched cortex, of course, the blood is excluded. But by the blanching renin is produced. The purpose of the production of renin is to raise the peripheral circulatory pressure so that the cortex may not be further and unnecessarily deprived of its blood supply. It is very easy to see how this in such an individual can occur and recur, and after a number of years it has its effect. This effect as regards the renal circulation—and this is quite well proved by Trueta in his various methods of examining the kidney—is the formation of a collateral circulation which is in fact a link between the juxtamedullary glomeruli and the venous circulation of the kidney. Thus we have a vascular by-pass which shunts the blood-flow from the cortex first of all only during the period of cortical spasm, but as years go on, through a more or less perfectly formed renal by-pass. When this has happened to a large degree there will be a sufficient continuous formation of renin to send the blood-pressure up permanently.

Arteriosclerosis is another factor which produces the more obvious microscopic and macroscopic changes in the retina, with permanent renal ischæmia, completely healthy renal tissue, and between the two in the same kidney partially diseased renal tissue.

This is a summary of what we know about the causative pathology of hypertension, and I should now like to show a figure which is an attempt to describe what happens clinically in a case of hypertension (see Bourne, G., "Hypertension—ætiology and surgical treatment", *Brit. med. J.*, 1948 (i) 435). Here (fig. 1) we have in the 'teens a

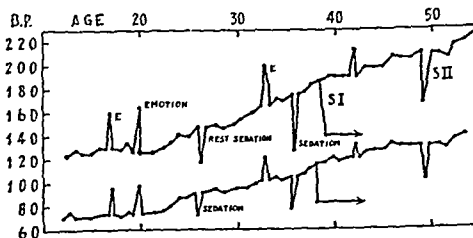


FIG. 1.—S.I indicates sympathectomy done before the onset of permanent renal damage. S.II indicates sympathectomy after renal damage has occurred. (From *Brit. med. J.*, 1948 (i), 436.)

normal limits, is nevertheless substantially improved and—this I believe is very important—less variable from day to day and hour to hour.

I would conclude by saying that although sympathectomy and splanchnicectomy may not cure the patient with complicated hypertension, nor possibly prolong life, yet there is a very good chance of relieving the symptoms, especially those of headache and impaired vision.

In two cases there has been some optic atrophy after the retinitis has subsided; in both patients the retinopathy had been present for a long time.

The great contra-indication to operation is the elderly patient with generalized arteriosclerosis in whom the body has lost its adaptability to a lowered blood-pressure and who is likely to die of coronary or cerebral thrombosis if not operated upon, and certain to die of these complications with the added risk of renal failure after operation.

Mr. A. S. Philips showed some fundus pictures of patients before and after sympathectomy had been performed by Mr. Tuckwell. He said: These patients have not been specially chosen, being simply those patients who presented themselves at a moment when I had an opportunity to make a fundus drawing. It is fortunate that the fundus camera and colour film will soon make the laborious art of fundus-painting unnecessary. I am very grateful to Dr. Geoffrey Bourne and Mr. Tuckwell for the opportunity afforded for observing the fundus changes in these patients.

Hypertensive retinopathy is a comparatively new term which has come to replace arteriosclerotic and renal retinitis, for it seems evident that in both these conditions the retinal changes are brought about solely by arteriolar spasm and long-continued high blood-pressure, and that when this high pressure is caused to fall within normal limits many of the retinal lesions disappear. I have not found any one type of exudate confined to a particular kind of case and furthermore the cotton-wool patches, which used to be thought typical of renal retinitis, may occur in hypertension from any cause.

The Americans have classified hypertensive retinopathy into four stages. The method is by no means exact as the age of the patient makes a difference in the hypertensive changes produced.

Stage I is minimal arterial narrowing. What we should describe as mild arteriosclerosis.

Stage II shows a more marked degree of this plus arteriovenous compression.

Stage III includes retinal œdema, exudate and hæmorrhages.

Stage IV shows papillœdema.

This papillœdema, as understood by the physicians, does not mean the low degree of retinal œdema spreading on to the disc, which we, as ophthalmologists, commonly observe, but the more defined and isolated swelling of the disc due to raised intracranial pressure following hypertensive encephalopathy.

It seems that this same papillœdema, as I understand it, marks the dividing line between a benign and a malignant hypertension. A case with papillœdema and no other retinal change is called malignant hypertension while one with retinal œdema, hæmorrhages and exudates is called a benign hypertension. Perhaps I have interpreted this distinction too literally, but, it seems to be a purely arbitrary one, and I know it is made because I personally observed over two years the eyes of a friend of active habits and no symptoms except for interference with vision due to retinal exudate and hæmorrhage. He died at the end of that time and only at the last was his condition described as malignant hypertension. It seems to me that retinal œdema and exudate are a portent of things to come as surely as is papillœdema due to encephalopathy, and should denote a malignant and not benign condition.

The following case is included to illustrate the end-condition of the retina in hypertension when relief of the hypertension is not possible.

Mrs. G., aged 40, was admitted to St. Bartholomew's Hospital in April 1941 with a six months' history of migraine, breathlessness and œdema of the ankles. On admission to hospital she had a tachycardia of 112 and blood-pressure of 260/200. A drawing was made of her fundus appearance on admission (fig. 1). There was a moderate degree of retinal œdema, though the choroidal pattern could still be made out, with a partial star figure at the macula. Arteriovenous compression and scattered hæmorrhage and exudate: a Stage III hypertensive retinopathy.

The macular star figure is a fairly accurate record of the degree of retinal œdema. The retina appears to be held down at the fovea to the underlying pigment layer, and as it is elsewhere free, lines of tension form which radiate outwards from the fovea whenever the retinal tissues become stretched by œdema. These lines of tension are a sign of retinal œdema from whatever cause, and may also be seen in thrombosis of the central retinal vein and in papillœdema due to intracranial neoplasm, though in this condition the macular fan is always partial and is confined to the area between the disc and the macula. These are not original observations but were made twenty years ago by Foster Moore.

Ophthalmoscopically the lines of tension are marked out by lines of white exudate and I do not know whether it is that the exudate occurs only along those lines, or whether it is deposited everywhere

typical of essential, or renal, hypertension imposes more strain on the heart and small vessels as seen in the retina.

The operation consists of removal of the tenth dorsal to first lumbar ganglia inclusive and the terminal portions of the splanchnic nerves. To be a complete denervation of the renal and celiac plexuses the operation must be more extensive and possibly include most of the thoraco-lumbar sympathetic chain. Several exposures of the splanchnic nerves have been described. The most extensive operations involve partial or complete division of the diaphragm, with resection of the sympathetic nerves in the thorax and abdomen. I prefer the approach through the pleural cavity, partially dividing the diaphragm from above and removing the lateral ganglionated chain from the fourth or fifth dorsal to the first lumbar inclusive; at the same time the splanchnic nerves are removed in their entirety. The operation is technically not difficult and exposure of the nerves and ganglia is good; any damage to intercostal vessels, usually veins, is seen and hæmorrhage easily controlled; the operation on one side lasts not more than an hour and the patients stand it well and are fit for the second side in two or three weeks.

I believe that we ought to operate early on those patients who are going to develop complicated, so-called malignant hypertension, but the difficulty of early diagnosis of this group is very great. Surgeons usually see them when retinitis or papilloedema or both are already present, or there is already severe renal damage. In the treatment of this disease it is essential that the physician, the ophthalmologist and the surgeon work together. I have had the great pleasure of working on this subject with Dr. Geoffrey Bourne and Dr. Graham Hayward and an expert opinion on the fundus of the eye has always been obtained from Mr. Rupert Scott or Mr. Seymour Philips. We use the grading of cases according to the retinal changes as described by Keith and Wagener:

Grade I: Normal or arteriolar constriction only.

Grade II: Tortuosity of the vessels and nicking of the veins at the arteriovenous crossings.

Grade III: More marked arteriolar change and retinitis (exudate or hæmorrhage).

Grade IV: Papilloedema usually with exudate or hæmorrhage.

Spontaneous regression of the retinopathy with disappearance of the œdema, exudate and hæmorrhage does occur with sedation and rest in a few patients, but after sympathectomy there is usually an immediate and often dramatic improvement even in patients who have received long and adequate rest in bed. Most of the patients with the worst eyes noticed a definite subjective improvement in their vision before they had left the surgical ward, that is to say within two weeks of the second operation. This improvement is remarked by the patient before my unskilled eye can detect an improvement in the fundus.

Changes in the eye caused by thrombosis of the retinal vessels always improve spontaneously I believe; one such patient of mine now has an almost normal fundus although the second part of the operation was not attempted on account of coronary thrombosis and her pressure is more or less unchanged.

A good renal function is desirable for a good operative risk; but I have operated on three patients with poor excretion and raised blood urea, with remarkable improvement in their general health and regression of the disease from Grade IV to Grade I. In these patients the renal function is not improved; one of them is now moribund one year after operation, he still has normal fundi and has enjoyed some months of comparatively normal life at work after being practically blind.

Analysis of my personal cases of complicated hypertension would be of little value as they only amount to 12, 9 of Grade IV and 3 of Grade III; but Professor Paterson Ross has very kindly allowed me to include his cases giving a total of 16 Grade IV and 6 Grade III.

TABLE I.—CHANGES OF FUNDUS AFTER OPERATION

GRADE IV

Regression to Grade III	1
Regression to Grade II	6
Regression to Grade I	4
Returned to Grade IV after 3 years	1
Died shortly after operation ..	1
Recent operation but improving ..	1

TABLE II.—CHANGES OF FUNDUS AFTER OPERATION

GRADE III

Regression to Grade II ..	3
Remained at Grade III ..	1
	(3 months)
Advanced to Grade IV ..	2
	(1 at 3 years, 1 at 8 months)

In addition two patients who had Grade II fundi at operation now have advanced to Grade IV, one three years and the other one year after operation.

In all those patients whose eyes have deteriorated the blood-pressure has not responded to treatment and the diastolic pressure is the same or higher than before operation.

In all those patients with improvement the blood-pressure, though seldom reduced to

The next picture (fig. 2) was painted in October 1947, i.e. six months' interval between pictures. This shows a disappearance of the hæmorrhage, exudate and œdema and some pallor of the disc. Collateral venous circulations have developed to overcome obstruction. His vision was 6/9.

He now writes that he is at work and his vision is good. Here again a very striking improvement is evident.

CASE III.—W. P., aged 23, male. First seen by me in St. Bartholomew's Hospital in December 1947, complaining of headaches and poor vision. Right vision was 6/18 and left was less than 6/60. Both fundi showed Stage III retinopathy with fairly complete star figures and moderate retinal œdema. He had a bilateral splanchnic neurectomy and I saw him again on January 21, 1948. There was still some retinal œdema but the blood-pressure had fallen to 170/110, and the exudate had become powdery, which is usually the last stage before disappearance. His vision had improved from right 6/18 to 6/6, and left 6/60 to 6/9 unaided.

I last saw him on March 1, 1948, when he was readmitted to Hospital under Dr. Bourne with some congestive heart failure from which he is now recovering. The fundi show hardly any exudate though there is still a little œdema. His blood-pressure is 160/100.

SUMMARY

Three patients, not specially selected, were described. All three complained of failing sight and in all there were such gross retinal changes that it seemed their vision must fail altogether before long unless some reduction in their blood-pressure could be achieved. The longest history of the three after operation is only a year, but all three have normal vision at this time, which seems to be a very remarkable thing considering the usual outcome of such cases.

Mr. E. F. King said it was surprising that patients with Stage IV hypertensive retinopathy rarely showed neurological disturbance. It might well be that the papilloœdema represented the terminal stage of generalized retinal œdema rather than the response to increased intracranial tension. In the few cases he had observed with gross papilloœdema there had been little improvement in the fundus condition following operation.

Mr. O. Gayer Morgan referred to a case which he saw over a year ago, with high blood-pressure, 240/160 and with Stage IV retinopathy. The patient, a student, had the first operation of sympathectomy on one side, and the next day he complained that one of his eyes was quite blind. He had been seeing about 6/18 with each eye. Now he had no perception of light in that eye at all. Mr. Morgan presumed that he had thrombosis of the central retinal artery, but there was no possibility of seeing the fundus changes in such a condition because it was masked by the extremely œdematous condition of the disc, macula and fundus generally.

The patient had his second operation three weeks later and he was now actually back at Cambridge engaged on his previous studies. On looking at his fundus he had complete optic atrophy on one side, with no perception of light. With the other eye he was able to see 6/6, but one was surprised that that was so in view of the irregularities at the macula and the extremely narrow arteries. Would it be a difficult thing to deal with the cervical sympathectomy at the same time? Would that in fact make his retinal arteries dilate and would it also help in preventing a thrombosis of the central retinal artery which had certainly occurred in this man.

Mr. R. W. Stephenson said that Mr. Philips had remarked upon the distinction between benign and malignant hypertension. Was there any real distinction between these two conditions? Was the second not merely an extreme degree of the first?

Mr. R. B. Terry said that the examination of the fundi was important not only for prognosis and diagnosis but also, one would like to think, because the condition of the fundi was a reflection of what was happening throughout the body. If these hæmorrhages took place in the fundi it was hardly conceivable that they should be only occurring there and not also in the kidneys and the heart. If that were true it would give a better indication of why things were going wrong elsewhere.

With regard to the ætiology of the hæmorrhages and the effect of sympathectomy on the retinal appearance, there might be another factor concerned, namely, capillary fragility. Capillary fragility had been shown to exist in quite a high proportion of cases—some 20% of hypertensives—and among those who showed this phenomenon there was an increased incidence of cerebral and retinal vascular catastrophes.

With regard to the effect of sympathectomy, it might be that if sudden and repeated rises in the level of the blood-pressure as mentioned by Mr. Tuckwell did not occur, the hæmorrhages also did not occur. It was possible that sympathectomy by some means also affected capillary fragility. That abnormal capillary fragility did exist in many hypertensives had been shown conclusively and it could be moderated by administering rutin. Sympathectomy

but only reflected from those points. In either case the rise and fall of retinal œdema can be gauged from the appearance and disappearance of the macular fan.

One month after admission there were additions to the star figure and on June 5—two months after admission—the next drawing was made (fig. 2).

There is a general increase in the œdema, as shown by the disappearance of the choroidal pattern and the increased blurring of the disc and we may now say that she has passed to Stage IV and has

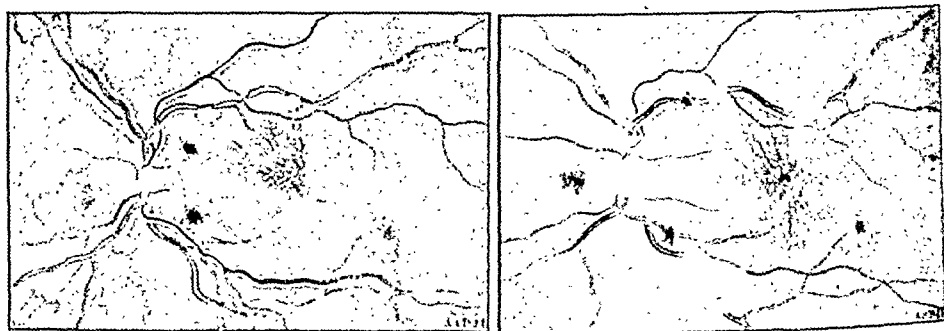


FIG. 1.—Retinopathy in a woman of 40. (Mrs. G.) Systolic pressure 260. FIG. 2.—The same eye 3 days before death of the patient.

papilloedema. The star figure is more complete and the central pit is deeper. She died of terminal congestive heart failure and pneumonia three days after that picture was made.

These drawings are shown here in order to heighten the contrast between the fate of this patient and that of those whose blood-pressure can be reduced by surgical means, viz. Cases I, II and III.

CASE I.—A. D., aged 25, was admitted to St. Bartholomew's Hospital in January 1947. Blood-pressure 230/150. The patient complained of misty vision, headaches and that he saw white lights as green with the right eye. His retina showed a true Stage IV retinopathy, with papilloedema and an early star figure. During February and March 1947 he had two operations for transpleural sympathectomy. I next saw him on June 12, 1947, when his systolic pressure had fallen to 175, and his right vision had improved to 6/9. The papilloedema had disappeared and there was only a trace of retinal œdema at the macula with the last remaining fragments of a star figure. The interval between the paintings of his right eye was therefore six months. On January 29, 1948, his blood-pressure was 175/110, right vision 6/6 unaided and there was no hæmorrhage, exudate or œdema in either eye. The retinal arteries remain very thin especially round the disc, as one would expect for it is not upon their nerve supply that the operation is carried out, and the disc is pale.

This seems to me a striking improvement, maintained over one year and not to be accounted for by rest in bed or other coincidental treatment.

CASE II.—R. M., aged 50. Admitted to St. Bartholomew's Hospital April 11, 1947, complaining of "bursting headaches" and a film over the right eye. His blood-pressure was 232/126. His right vision was 6/36. In May and June 1947 he had bilateral splanchnic neurectomy and he left hospital on July 8, 1947. His blood-pressure on discharge was 150/100, but rose to 170/110 later. On admission he had shown a Stage III retinopathy, with a solid-looking œdema at the macula and no

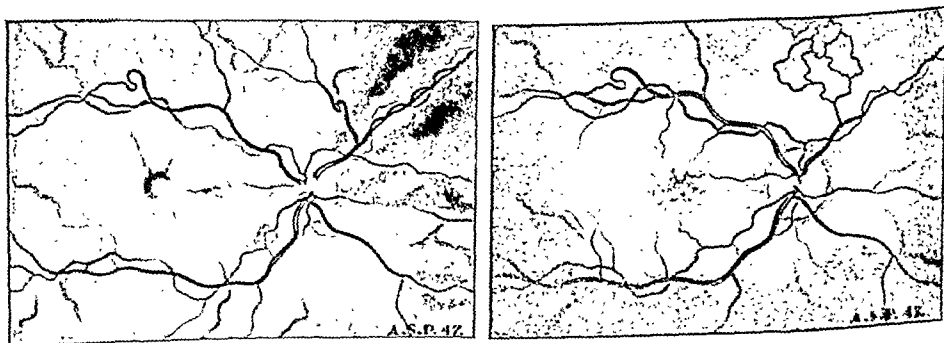


FIG. 1.

FIG. 2.

CASE II.—R. M., male, aged 50. } Right fundus before (fig. 1) and after (fig. 2) sympathectomy.

star figure. There were many venous hæmorrhages due to compression of the vein at the arterio-venous crossings, and the constriction of the arteries at and near the disc was very marked (fig. 1).

Section of Medicine

President—MAURICE DAVIDSON, M.D.

[April 27, 1948]

DISCUSSION ON GENERALIZED DISEASES OF BONE IN THE ADULT

Dr. E. F. Scowen: *The effects of some hormones on osteogenesis.*—In order to make clear the subsequent discussion I will first review briefly the main steps in the formation of bone.

In endochondral bone formation, there is first proliferation of cartilage cells with an increase in intercellular substance and an arrangement of the cells in order. This is followed by calcification of the intercellular substance and the breaking through of blood-vessels into the areas containing the cartilage cells. Osteoid tissue is then laid down by the osteoblasts on to the surface of the calcified areas and into this osteoid is later deposited calcium and phosphorus complex.

Membranous bone is formed directly from a specialized tissue without preceding cartilaginous phase, and for the purpose of discussion this term as suggested by Fuller Albright will also be used to include periosteal bone.

I will use the term endosteal bone formation for bone laid down in the cortex and trabeculae of bones which occurs both during skeletal growth and throughout adult life, and I would like to point out that the final stages in all varieties of bone formation are essentially the same, namely the formation of bony matrix by the osteoblasts and the deposition of calcium and phosphorus in this matrix.

This definition of osteogenesis is, of course, over-simplified, but I have used it so as to be able to demonstrate the selective effect of some hormones on the different phases of osteogenesis. It will also be clear that the formation of bone, namely the formation of osteoid can be separated from calcification of this osteoid and this allows us to adopt a classification which may clarify the essential differences in three types of disease which are characterized by a deficiency of calcified bone. Thus, osteoporosis is used to designate any condition in which there is a decrease of bone due to a failure of osteoblastic activity and an insufficient quantity of osteoid formation. Such osteoid tissue as may be formed is normally calcified. Such a condition would not arise from a disturbance of calcium and phosphorus metabolism but from a true disturbance of bone growth. In such conditions, therefore, the serum calcium and phosphorus levels and the alkaline phosphatase are normal.

In the condition of osteomalacia, which arises as a result of a disturbance of calcium and phosphorus metabolism the bone is softer than normal owing to the failure of mineralization and this results in excessive osteoblastic activity. In contrast, therefore, to osteoporosis there is an excessive quantity of osteoid tissue elaborated and a deficient deposition of calcium and phosphorus in this matrix. The serum calcium and phosphorus vary with the severity of the condition but the phosphorus level is usually depressed and the alkaline phosphatase in the blood invariably increased.

In conditions of osteitis fibrosa generalisata, most commonly the result of hyperparathyroidism there is excessive resorption of bone which is accompanied by excessive osteoblastic activity. As a result of the over-action of the parathormone and the osteoblastic response to the bone resorption, there is a high serum calcium, a low serum phosphorus, and a high alkaline phosphatase.

The Effects of the Growth Hormone on Osteogenesis

I do not propose to discuss the evidence on which the identity of the growth hormone is established but to review briefly the clinical manifestations of alterations in the production of the growth hormone from the anterior lobe of the pituitary. It is difficult, of course, in many cases to distinguish the effects directly as the issue is often clouded by interference with the elaboration of other hormones at the same time. Nevertheless some clear-cut deductions emerge as a result of this study.

The failure of growth hormone production can occur as a result of pituitary destruction.

As an example here is a patient with a suprasellar cyst. Symptoms date from the age of 5; she is now 16 years old and is the size of a child of 7 or 8. The X-rays show a bone age of 9 and the epiphyses are all open but the bones otherwise would appear quite normal for the age of 9 and there is no suggestion of osteoporosis. The 17-ketosteroid excretion is in the normal range for a pre-adolescent child. There has been a failure of epiphyseal growth but endosteal replacement has not suffered.

There is another condition of dwarfism which is associated with anterior lobe failure. This is commonly called panhypopituitarism. In such cases all functions of the anterior

must be causing some change other than merely the reduction of blood-pressure, since in certain cases, in spite of the blood-pressure going up, there had been no return of the hæmorrhages.

The President asked what was the relationship between arteriosclerosis, hypertension and the kidney condition. In how far were these separate entities dependent on each other and what was the causal relationship between them.

Dr. Geoffrey Bourne said, in answer to the President, he would suggest that hypertension was a separate entity from arteriosclerosis, and that in those people whose arteries were liable to degenerate the hypertension would inevitably accentuate the arteriosclerotic changes. But hypertension might be present alone, certainly for twenty years, as in coarctation cases, and in other individuals who had hypertension for a long time without any clinical signs of actual arterial change. Therefore arteriosclerosis, he thought, could be definitely said not to cause hypertension. Hypertension certainly would accelerate changes.

With regard to the other points, he thought that the reason why one did get clinical information that an individual with a Stage IV change in the retina had apparently been perfectly well until quite recently was that such cases were far more commonly renal than hypertensive. These individuals had been apparently well until they came up to the ophthalmic department with loss of vision. There were a few cases of hypertension in elderly people who certainly manifested a Stage IV change in the retina. In some there had been quite a long history and the explanation of that was the difference in the aetiology of the two types.

As to whether there was any essential difference between benign and malignant hypertension, these were just useful labels, and not anything more. He would say that an individual had malignant hypertension when he had arterial retinal changes with papilloedema and that in most of such cases the progress of the disease had been accelerated, so that there was a story of continuous deterioration. Finally, most of such cases were rather young—not middle-aged.

Dr. Terry's statement about the possibility of fragility of the capillaries was an interesting one. He would stress again that there were two quite distinct things—there was hypertension and there was also a factor which caused the blood-vessels to become vulnerable to the effects of hypertension. That was something separate and distinct. It was frequently not present for many years, but after all everyone degenerated physically as he grew older, and the young individuals with nephritis unfortunately got a similar sort of change much earlier in life. Therefore the change in the blood-vessels was an extremely important and quite separate problem.

Mr. E. G. Tuckwell, also in reply, said that the term "malignant hypertension" was a bad one. It would be much better to use the term "complicated hypertension". He agreed with Dr. Bourne that it was all one disease, and it could be called complicated when there was retinopathy and other eye changes.

Mr. A. S. Philips, in reply, said that Mr. King had raised the question whether Stages III and IV were the same thing or degrees of the same thing. While he was not sure on that point he thought that in some cases Stage IV was different, as there was present in it not only hypertensive changes in the retina but a type of papilloedema which denoted a space-taking lesion in the skull. One of the pictures shown accompanying his paper did bring out this point.

Mr. Philips recalled that Mr. Paterson Ross and Professor Gask had carried out a cervical ganglionectomy at St. Bartholomew's Hospital. Mr. Foster Moore had been asked to see the patient afterwards and he had declared that he could not see any enophthalmos or difference in the calibre of the retinal vessels on the two sides.

effects of oestrogens on the skeleton of birds and mice. It appears probable that such experiments may help to elucidate the peculiarities of the skeletal distribution of bony abnormality since the same oestrogen may produce dissolution of one bone and yet proliferation in another bone.

The excessive skeletal growth in girls in association with granulosa-celled tumours of the ovary and the stimulation of growth sometimes seen in cases of ovarian agenesis under the influence of oestrogens suggest that the oestrogen itself may have a direct stimulating effect on epiphyseal growth. This, however, is not certain as it is impossible to prove at present that such effects are direct and are not mediated through secondary adrenal response. This latter effect has received some experimental support and further indirect support as we shall see in the discussion of the effects of the adrenal cortex on bone formation.

There is no doubt that oestradiol can affect the calcium balance and has been shown to reverse the negative balance in post-menopausal osteoporosis and in osteoporosis with Cushing's syndrome. Such change was produced without any appreciable effect on nitrogen metabolism.

Oestrogens can therefore undoubtedly influence the calcium balance and appear to influence endosteal bone growth. They may stimulate endochondral bone but like testosterone are not capable of producing excessive bone growth.

The Effects of the Adrenal Cortex on Osteogenesis

There is no doubt that the adrenal cortex profoundly influences bone growth but it is difficult to elucidate these effects from a gland as complex in its functions and which appears able to produce contrary actions.

I do not propose to discuss adrenal function and I will have to assume the acceptance of the conception of two main actions of the cortex through two groups of hormones, one of which has an androgen-like and the other a corticosterone-like action.

The adrenogenital syndrome is a demonstration of the androgenic action of the adrenal cortex. Children with this syndrome show rapid skeletal growth which is terminated early by the effect on the epiphyses and their early closure, frequently resulting in deficient height. Once epiphyseal closure is complete bone growth ceases and excessive bone is not produced. Indeed in the adult who develops this syndrome no bony change is seen. The children may show some slight growth in height after long bone epiphyses have shut and this is due to vertebral growth which may persist for many years.

This acceleration of endochondral growth and lack of excessive endosteal or periosteal bone closely resemble the effects produced by testosterone and it is in this syndrome that the excretion of 17-ketosteroids in the urine is always markedly increased.

The primary disturbance in Cushing's syndrome is still a matter of argument but there is no doubt that there is a gross derangement of the adrenal cortical function. The urinary excretion of 17-ketosteroids may be somewhat increased but this is inconstant and seldom of any magnitude. The excretion of corticosteroid substances is always increased and often remarkably so, both by biological and chemical assay.

In Cushing's syndrome in contrast with the adrenogenital syndrome, bone growth is remarkably retarded and epiphyseal growth may cease altogether. In addition there develops a remarkable thinning of the spine and often of the pelvis. The structure of such bone shows a failure of osteoblastic activity, the condition of osteoporosis.

From the experimental observation that both corticosteroid-like substances and the adrenocorticotrophic hormone can prevent bone growth in animals, and indeed can abolish the effects of injected growth hormone, it seemed reasonable to assume that the bone disorder in Cushing's syndrome might be brought about by an excessive production of corticosteroid substances which we know to be occurring. This effect is in direct contrast to the action of the sex hormones and is thrown into contrast even more by the persistent negativity of the nitrogen balance, independent of the nitrogen intake. This effect can only be overcome by a gross excess of testosterone.

With this osteoporosis the calcium and phosphorus in the blood are normal and the alkaline phosphatase is usually stated to be normal. Such findings are usual in osteoporosis. In Cushing's syndrome, however, it is not invariably true and in the patient I have chosen to illustrate this disease a high alkaline phosphatase was constantly found during the time the vertebrae were markedly deteriorating.

Osteoporosis in the spine and pelvis are the bony features of this disease and appear to be explained by an excessive production of corticosteroid-like hormones from the adrenal cortex. These substances interfere with, or prevent, osteoblastic activity as part of the general interference with tissue anabolism and in consequence no bony matrix is formed. This process is especially marked in the spine and pelvis and growth of the epiphysis is also inhibited. If therefore it is accepted that these changes in Cushing's syndrome are the result of over-production of corticosteroid products the adrenal is capable of inhibiting both endochondral and endosteal bone formation.

lobe are deficient. Untreated, such patients grow at a very slow rate but growth persists indefinitely since they do not reach complete sexual or skeletal maturity. Under treatment with testosterone and thyroid, growth may be markedly accelerated provided over-enthusiastic use of testosterone does not lead to epiphyseal closure. Over-dosage, however, does not lead to excessive bone formation and the effect of the treatment is shown almost entirely in epiphyseal growth, that is endochondral bone formation, and may be akin to the effect seen in animals in whom after hypophysectomy, treatment with testosterone prevents the cessation of bone growth and enhances the action of injected growth hormone.

The syndromes produced as a result of increased growth hormone production occur with eosinophilic hyperplasia or neoplasia of the anterior lobe. Acromegaly occurs when this process begins after skeletal maturity. The osseous manifestations are produced by an excessive periosteal bone formation but in certain sites further endochondral bone is stimulated. The cartilaginous end-plates of the vertebræ start to undergo hyperplasia and this, together with periosteal bone formation, produces the remarkable changes in the vertebræ which seem to be always most marked in the region of the lower thoracic vertebræ.

Gigantism results when the disease begins before skeletal maturity but the stimulation of endochondral and periosteal bone is uniform and disproportion is not evident as in the restricted response of acromegaly. Growth can proceed indefinitely if epiphyseal closure does not occur.

It is clear that in the early stages of gigantism, before pituitary function is completely disorganized the changes of puberty may occur. If this should happen the features of pure gigantism will be clouded by a superimposition of acromegalic features, once epiphyseal closure has occurred in the long bones under the influence of puberty.

Lastly I would like to draw attention to a syndrome which has received little attention. It has no name and I will therefore refer to it as adolescent gigantism. Sometimes there is evidence of a pituitary tumour and sometimes not. Growth occurs rapidly for a short and limited time but usually ceases before the condition can reasonably be termed gigantism. Commonly sexual maturity fails to develop but often failure is incomplete. In man such a syndrome is commonly overlooked and appears to be compatible with reasonable health at least for many years until revealed later in life by complaints of maldevelopment, impotence or infertility. Further examination often shows, however, signs suggestive of pituitary failure. The testes are usually atrophic and show lack of spermatogenesis. Anaemia, though often mild, is intractable, and cardiac disease may later supervene and prove fatal, frequently with arrhythmia, often auricular flutter. Union of epiphyses in the long bones is often delayed but eventually occurs.

In view of the identity of these cases whether evidence of pituitary enlargement is demonstrated or not it seems reasonable to suppose that they represent a comparatively transient phase of eosinophilic adenomatous enlargement of the anterior lobe and the ultimate fate of such a patient is dependent on the degree of pituitary destruction which may occur during this time. Many such cases seem to masquerade later in life under the titles, in bad cases, of chromophobe adenoma, or in milder cases of Klinefelter's syndrome.

I have not seen in such patients evidence of osteoporosis in contrast with many cases of acromegaly who eventually show decalcification of the skeleton.

The osseous manifestations of these diseases show that in man the growth hormone has a stimulating effect on both endochondral and membranous, including periosteal, bone formation. There is little to suggest a direct effect on endosteal bone. The decalcification sometimes seen in acromegaly is at present unexplained. The inconstancy of its appearance, together with its absence in conditions of lack of growth hormone would suggest that it is associated with some indirect effect and related to other forms of osteoporosis which I will discuss later.

The Effect of the Sex Hormones on Osteogenesis

The skeletal effects of the testis hormone are well known and the failure of physical development as well as sexual development in eunuchs does not need elaboration here.

Since the use of testosterone, however, it has been possible to demonstrate conclusively its metabolic as well as its sex functions. I have already referred to the effects of testosterone in panhypopituitarism and the effects on bone growth in hypophysectomized animals, but at this point I would like to make it clear that such changes are not isolated but occur in association with somatic growth generally, and the development of a positive balance, not only of calcium and phosphorus, but in particular of nitrogen. These effects of testosterone are exerted in all tissues and growth is accelerated. Such growth includes epiphyseal growth and also endosteal and probably periosteal bone growth, but unlike the effects of the growth hormone the response is limited and uniform and excessive bony response cannot be produced.

The effects of the oestrogens on the bones seem to be similar to testosterone but the oestrogens lack the somatic effects and the available data is far from conclusive. Considerable work in this field has been stimulated by the demonstration of the remarkable

of the conditions show phases in which the bones exhibit first one and then the other type of reaction.

Decalcification

Osteoporosis, &c.—The most important in the radiographic diagnosis is that found in hyperparathyroidism. It has been claimed by certain workers (Snapper, 1943) that in more than half of the patients with hyperparathyroidism the predominant symptoms originate from the urinary tract and that the biochemical syndrome of the disease has been detected when the X-rays of the skeleton showed completely normal findings—Albright recorded that "in 15 of 35 consecutive cases of hyperparathyroidism no radiographic changes could be found—the symptomatology of these cases was exclusively renal in character". Yet in the cases of hyperparathyroidism submitted to me which have remained unsuspected though previously subjected to considerable clinical investigation, in some cases for three or four years, the radiographs have shown the typical distinctive evidence of the disease. Consequently I regard the radiographic diagnosis of hyperparathyroidism as of great importance. The diagnosis of hyperparathyroidism was not made for the average of 4·8 years from the onset of symptoms in some 49 cases recorded in the literature. This is very important because it was often not made until the destructive bone changes had resulted in multiple deformities due to fractures and abnormal plasticity of the bone, which could not be corrected even though the causal parathyroid tumour was removed. Early diagnosis and treatment permit the skeleton to return to the normal and avoid crippling deformities. Another reason for the delay has been the belief that the characteristic radiographic feature was osteitis fibrosa cystica—a condition which may not be seen in some cases in the early years. This belief has also been responsible for a large number of erroneous interpretations of the radiographic features.

Radiographs showing localized expansion of bone with obliteration of their normal cancellous structure—the conditions now referred to as polycystic dysplasia or polyostotic fibrous dysplasia—have been interpreted as examples of hyperparathyroidism. Histological evidence of osteitis fibrosa cystica, though this is but a type of reaction found in a number of different conditions, has been sought and obtained in some cases before surgical search for a parathyroid tumour which it was thought to indicate. Fortunately the radiographic appearances of the dysplasias are characteristic and their recognition should obviate such surgical explorations. The chief distinctive feature of these dysplasias as shown in the bones of the hand is the localization of the aberrant tissue in a segment of bone which was otherwise normal in size, structure and density. On the other hand the cystic conditions of the bone which may be present in hyperparathyroidism are associated with generalized osteoporosis; further, such lesions are usually multiple and do not show the tendency to unilateral distribution which is seen in the dysplasias. Because in hyperparathyroidism every part of the skeleton shows osteoporosis of a characteristic nature there is no need, as we too often see, for radiographic examination of the whole skeleton.

Radiographs of the hands in hyperparathyroidism show general decalcification of the bones: the phalanges are without compact tissue, the periphery showing in part the crenated surface of the cancellous tissue. The terminal phalanges in particular show a great degree of decalcification, the terminal tuft may be almost invisible. One or more of the bones may show one or more small areas of cancellous destruction—the representative of the "cysts" or giant-cell tumours in the larger bones. The bones of the forearm also show lack of compact tissue and a characteristic stippled osteoporosis, with areas from which the cancellous pattern has been wiped out. There is no other condition which presents these characteristic features in combination. True, in certain grave cases of so-called renal osteodystrophia there is a near approach but in these cases the parathyroids are probably responsible, for it is found that they show general hypertrophy. The long clinical history, in particular the continued prominent evidence of renal insufficiency, assists the differentiation. A lateral radiograph of the skull would also help, for though in the old-standing renal osteodystrophy, the skull may show the features of irregular ossification and calcification, the relatively recent case of hyperparathyroidism due to tumour would show a fine stippled osteoporosis with obliteration of the outline of much of the outer table.

Radiographs of the pelvis or long bones show in addition to the general osteoporosis large areas within which all the detail of cancellous structure has been wiped out with attenuation of the compact tissue to linear dimensions. In some cases the "cysts" are more clearly defined and expanded beyond the normal. With removal of the responsible parathyroid tumour the long bones recalcify and become of normal structure except in the larger cystic areas. These may retain a multilocular cystic appearance; one or more may become densely calcified. It used to be claimed that the radiographic features of hyperparathyroidism and Paget's disease were indistinguishable, but I trust that this belief no longer prevails, for the essential features of Paget's disease, even after a duration of twenty or more years, is its localization to certain bones of the skeleton. The radiograph of the

Senile Osteoporosis

Osteoporosis in man occurs in a variety of conditions. I have already considered Cushing's syndrome and I will not now say anything about disuse atrophy, extreme senility, or chronic inanition. I would like to discuss briefly the changes which are still called senile osteoporosis, although in many such patients their general condition and actual age belie such description. I think under this title three conditions can be distinguished: (1) Menopausal or post-menopausal osteoporosis; (2) pre-senile osteoporosis; (3) an idiopathic group at present quite unexplained.

The first two conditions have many similarities but I have separated the post-menopausal cases as this condition is for obvious reasons better defined in women and seems to be an exaggeration of the normal post-menopausal state. A lack of oestrogen is present and the decline in 17-ketosteroid excretion with increasing years would suggest a decline in the production of androgenic substances.

It seemed probable that the failure of sex hormone production both gonadal and adrenal might be a precipitating factor in the failure of osteoblastic activity. The administration of both oestradiol and testosterone has confirmed this impression, both in post-menopausal and pre-senile osteoporosis in men. Both compounds can make the calcium balance positive but the combined use is more effective than the sum of the two separately. The use of oestradiol alone appears not to influence the nitrogen but testosterone profoundly affects it and will produce a positive nitrogen balance with increase in weight and strength. It is not yet clear how much change will be produced eventually in the vertebral column by this therapy but the immediate results have been very satisfactory and it remains to be seen how much radiological change will be evidenced in the years to come.

Dr. James F. Brailsford: The scope indicated by the title of this Discussion is a wide one. Unfortunately the time allowed will not permit me to deal comprehensively with any of the groups into which I have classified the diseases.

The classification I have adopted is as follows:

(1) Generalized changes in bones due to dysplasias and dystrophies of the skeleton. These are essentially laid down in foetal or infantile life in varying degrees of severity. Some at one end of the scale are incompatible with a separate existence, others of much less severity permit of apparently normal life, even to old age, and then perhaps are only discovered by radiography during investigation for fracture, &c. These are few and far between and of importance only in the differential diagnosis; they include certain cases of osteogenesis imperfecta (Brailsford, 1943) and Albers-Schönberg's disease.

(2) Generalized bone changes associated with defects in other systems. These include renal and gastro-intestinal osteodystrophies and such conditions as von Recklinghausen's neurofibromatosis. The adult members of this group are usually known to have carried the disorder from earlier years.

(3) Generalized bone changes associated with deficiencies, endocrine and blood disorders such as osteomalacia, hyperparathyroidism, leukaemia and anaemia. These, as well as those in the succeeding groups (4) and (5), are the most important and most common conditions. They appear to be initiated in adult life and produce generalized changes in the skeleton which was formerly apparently normal.

(4) Those generalized diseases of bones which represent the terminal stage of diseases, which throughout the major part of their course have appeared as localized conditions and failed to respond favourably to any form of treatment administered. They include Paget's disease, syphilis, the solitary and the endothelial myeloma (Ewing's tumour) and carcinoma.

(5) Those generalized diseases of the bones which are associated with general progressive clinical deterioration. These conditions are often associated with long latent negative radiographic periods so that radiographs for many months may fail to show any changes in the bones and even when the changes do appear they may not be distinctive. These conditions are often classified under the title of senile osteoporosis of bones but more careful examination may permit of the recognition of myelomatosis, carcinomatosis or some serious disturbance of metabolism or endocrines.

Generalized diseases of the bones can be indicated by radiographs of any and every part of the skeleton; consequently radiographs of the hand are the best for obtaining indication of generalization. Because of the intimate contact between the radiographic film and the bones of the hand the detail of the bony structure is sharp and clearly defined. As a student I was impressed with Wood Jones's "The Principles of Anatomy as Seen in the Hand" and I suggest that a companion volume "The Pathology of the Skeleton as Seen in the Bones of the Hand" could be of equal value.

Radiographically we may consider these conditions of the adult skeleton under two main distinctive radiographic features, i.e. (1) diminished density of the bone—decalcification, and (2) increased density of the bone—osteoplasticity or osteosclerosis; though some

and appearances in the cretinoid form of the hands indicating that the changes are of many years' duration, probably associated with severe metabolic disturbances rather than infiltration with tumour cells.

There are a number of conditions in the adult skeleton which are associated with osteoporosis; often revealed by radiography which is being used to ascertain the cause of pain in the back or lower extremities. Compression fractures of one or more vertebral bodies, usually in the mid-dorsal or dorso-lumbar areas, are found. Usually these have been produced without any definite trauma: the pain may have come on suddenly when the patient was bending to pick up an object of no great weight; in other cases a more definite strain has been imposed at the time. The discs are expanded and the osteoporosed bodies are compressed to accommodate them. Radiographs of the hand may show a degree of general osteoporosis of no characteristic pattern. In many of these cases the underlying cause cannot be found and they are referred to under the term *senile osteoporosis*; in others, disturbances of the gastro-intestinal tract, diffuse myelomatosis, carcinomatosis, hyperthyroidism, pituitary or adrenal tumours or even syphilis may be found to be the cause.

Myelomatosis may occur subsequent to the development of a localized myeloma, but more often the disease is revealed in radiographs by multiple, small, well-defined, circumscribed areas of cancellous structure up to the size of a pea. These may be scattered about in the expanded ends of the main bones of the extremities, and in the pelvis, ribs and skull. Near the termination of the illness these foci may be almost contiguous. In the shafts of the long bones the cancellous tissue may be destroyed, the medulla expanded and the inner border of the compact cortex may show much crescentic scalloping of the size indicated above. In some of these lesions the peripheral border of the cortex may be pushed out beyond the line of the shaft. In those cases of diffuse myelomatosis the diagnosis may depend entirely upon the finding of Bence-Jones proteose and the recognition of the typical cells in the tissue removed by sternal puncture.

Carcinomatosis producing generalized osteoporosis of the skeleton is relatively rarely diagnosed at the stage when investigations are being made, though it is not so rare as a terminal observation. More commonly the disease is shown only in the pelvis, spine, ribs and proximal bones of the extremities and in these there may be irregular distribution. Even when the disease can be recognized radiographically as generalized in the trunk and proximal extremities, the bones of the hands may show only generalized osteoporosis. In a few cases only a single metastasis in one of the bones has been found and that in one of the bones of the hand—this may be the first indication of malignant disease. A radiograph of the chest may show the primary to be an epithelioma. Other lesions of the skeleton may be revealed after a variable period.

In *leukæmia* and in certain malignant tumours we may see a generalized osteoporosis of the skeleton with periosteal accretions along the shafts of most of the long bones simulating hypertrophic pulmonary osteoarthropathy; in other cases only localized sites of periosteal reaction are shown, with perhaps some disintegration of the underlying bone. In hypertrophic pulmonary osteoarthropathy due to abscess or neoplasm of the lung, regular periosteal accretions may be found enveloping all the long bones except the terminal phalanges, which though associated with marked clubbing of the fingers often show no change.

The possibility that the generalized osteoporosis associated with one or more spontaneous fractures is due to syphilis must not be overlooked. Radiographs of the skeleton in syphilis may show generalized blurring of the detail of all bones; the details of the diploë and the cancellous structure of the bones may be completely obliterated. Considerable absorption of the bone may occur at fracture sites, and this may not show any regeneration though the other bones respond well to appropriate medication. Generalized granuloma due to lipid and other abnormal cell metabolism may produce somewhat similar changes as I have described (Brailsford, 1948a). Certain cases of osteogenesis imperfecta live to old age and they may show evidence of multiple fractures; in some cases which I have seen, fractures have remained ununited for fifty or more years. The distinctive radiographic features I have recorded (Brailsford, 1948b). Fractures and compression of multiple vertebral bodies, pressure deformities, particularly of the pelvis and lower extremities, and a skeleton lacking in normal structure and density are usually found in any extensive examination; but the clinical history usually provides the key to the diagnosis. The occurrence of extensive subperiosteal hæmatoma as a complication of osteogenesis imperfecta must not be overlooked, for such have been mistaken for sarcomata. The generalized osteoporosis which is associated with hyperthyroidism need only be mentioned for the symptoms of the latter dominate the picture.

Osteoplasticity

There are a number of terms which indicate a diminished density of the bone, but few which denote an increased density. The terms *osteosclerosis* and *osteopetrosis* suggest a bone of stony hardness, but many of the bones to which they are applied have little more than the hardness of chalk. Because such bone often shows a greater degree of

hand, even in cases exhibiting the characteristic features of Paget bone throughout the skull, spine, and the large proximal bones of the extremities, may show all the bones of the hand to be normal, or one or two small bones may show the characteristic Paget bone throughout. I have classified (Brailsford, 1938) the radiographic features of Paget's disease into three types: (1) Osteoporotic; (2) Osteoplastic; and (3) Lithocystic.

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The Paget lesions in the long bones may begin with the appearances of a gradual deposition of calcium which obliterates the detail of the cancellous structure converting it into a so-called "ivory" bone of uniform density, but at the expense of increased fragility. Later the affected bone may show osteoporosis. When fracture occurs this osteoporosis becomes the noticeable feature. In other cases the lesion begins, as I (Brailsford, 1938) have shown, in a superficial lanceolate area of decalcification which gradually spreads along the bone in a very characteristic fashion; it produces what I have described as the V-shaped thrust of the Paget bone into the normal. The appearances can be illustrated by partially tearing the wrapper from a tightly covered journal, the end of the tear has the shape of a V. Such appearances suggest that the periosteum resists the progressive expansion of the Paget bone for a time, but eventually it yields, and strips in this fashion from the adjacent normal bone. The line of demarcation is clearly defined, the Paget side showing decalcification by its lesser opacity than the normal. As the acute phase passes, the line of demarcation may be removed and the two segments may blend or a further recurrence may occur and the Paget thrust be extended to involve a further segment or the remainder of the bone. This characteristic V-shaped demarcation between the normal and Paget bone is to be seen in no other condition. Obviously it could not be present in a condition which is generalized, yet the literature contains illustrations showing this characteristic feature of Paget's disease labelled Fluorosis. Spéder (1936) used such an illustration and labelled it "Fluorosis".

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(The radiographs used to illustrate this paper are to be found in Brailsford, 1948a.)

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Sir Thomas Fairbank: I propose to refer to a few somewhat unusual cases.

Occasionally osteogenesis imperfecta may be a matter of real interest in an adult patient. It is well known that some cases, particularly the milder ones, tend to improve gradually, till the fragility of the bones disappears. Occasionally recovery may take place even after adult life is reached.

A rather severe pre-natal case never walked till 12 years of age, and was laid up with many more fractures later. There was an element of softening of the bones or mollities present, in addition to the fragility. At 20 there was still considerable generalized osteoporosis and an incomplete fracture of one femur. This young woman, although a deformed dwarf of 31, is able to get about and has worked as a secretary in a London office for some years. One brother, in a family of four, was also affected: he died at 17, never having walked.

There is a rare and little-known complication of osteogenesis imperfecta which may occur in the adult. It is not only of considerable interest but is important from the diagnostic point of view.

A boy aged 14 in 1937 had had multiple fractures early in life but none for the preceding six years. When 7 the right thigh had been contused, and at 8 thickening of the thigh was noticed. Amputation of the leg had been seriously considered. Radiographs taken in 1937 showed a large amount of open mesh bone surrounding the lower two-thirds of the femur. Now at 24 recent films show the additional bone still present. At 14 there were signs of a fracture of the shaft of the left femur, united with no excess of callus. Ten years later he suddenly complained of pain and swelling of his left thigh. A radiograph five weeks later showed a shadow measuring at least five inches across in the film, and its shape and texture suggested the possible presence of a sarcomatous growth. Fortunately we have experience of other cases that have developed similar masses of hyperplastic callus.

Dr. Brailsford, in a paper on osteogenesis imperfecta (1943) referred to four cases complicated by what he took to be superiosteal hæmorrhages, and he suggested an element of scurvy to account for these. His cases include the one now referred to, copies of the early records and films having been also sent to me by Dr. W. Mackenzie, to whom I am indebted for the recent history and further radiographs.

In 1946 Professor S. L. Baker published a paper on "Hyperplastic callus simulating sarcoma in two cases of fragilitas ossium". We now have records of six other cases (Fairbank and Baker, 1948). Most, but not all, of the eight cases have a background of osteogenesis imperfecta.

The femur is the bone most frequently affected. The hyperplastic callus, with or without a provocative fracture, may, as in this case, extend the whole length of the shaft of the bone. Sometimes the early callus is excessively dense and structureless. Another feature of these cases is the presence of multiple bony excrescences on the shafts of the long bones, particularly along the interosseous borders of the bones of the forearm and leg. Professor Baker has informed me that one of his cases in which, as a result of fractures four years ago, both femora were surrounded throughout their entire length by enormous masses of callus, has also recently flared: at the age of 19 he has developed, quite spontaneously on this occasion, great swelling of one thigh and a new mass of callus. For various reasons we cannot agree with the suggestion of scurvy: histological examination of biopsy specimens in Baker's two cases revealed no sign of old hæmorrhage. Sections showed infiltration of the muscles by oedema and chondroid tissue, while in the deeper layers of the mass there was calcified cartilage and woven bone. Similar histological features were found by Professor Baker after a recent biopsy in Dr. Mackenzie's case. The callus in this case increased still further in thickness and extended the full length of the bone, but now the swelling has begun to subside. It seems highly probable this femur also will remain permanently enlarged. But for the curious behaviour of his two femora, this case seemed to have recovered from his generalized osseous dysplasia.

X-ray films were then shown of an old lady of 73 suffering from osteopetrosis or "marble bones". On admission to hospital (under Dr. Wallace J. Gill) with a minor head injury, the extreme density of the bones and an old fracture of one femoral neck were discovered. Though the generalized osteopetrosis was very severe, there was no anæmia, and no optic neuritis. Spleen not palpable. The

moulding than the normal and for the want of a better term, I have used the term osteoplastic. Generalized osteoplastic change throughout the entire adult skeleton recognizable by radiography, is rare. From time to time one sees a case of Albers-Schönberg's disease in an adult. Such cases are recognized from radiographs taken in the course of investigation of fractures or other conditions. Though the condition may not be recognized until middle or late life it has been present since infancy and would have been detected at an earlier age if radiographs had been taken. In some cases the condition can be recognized in the fœtus *in utero*, in others the dystrophic bone commences to be laid down in infancy. As with other general dysplasias and dystrophies of the skeleton it may be so severe as to affect the fœtal skeleton seriously and be incompatible with survival; such cases can be detected by radiographs of the pregnant woman. In other cases severity permits of life for a variable period—even to old age—and the dystrophic bone maintains its characters. In the severe degrees of the dystrophy, the dystrophic bone laid down is expanded beyond the normal, giving the long bones club-shaped extremities and the vertebral bodies an expanded denser superior and inferior third. All detail of the structure of the skull may be obliterated so that the radiographs suggest an earthenware skull. In the lesser degrees, and it is these which are discovered accidentally only by radiography, some of the bones may show little departure from the normal shape, though they show little true compact bone and bands of dense bone running parallel to the growth cartilage with little or no evidence of a medulla. Such bones fracture like chalk—the fibrous element being apparently deficient. The nature of the condition may be brought to light because of such a fracture or because of a progressive anæmia or cranial nerve involvement. The radiographic features are distinctive but apparently not generally understood for when Flemming Møller (1934) published his account of the appearances of the bones in fluorosis a number of papers followed on the subject in which the authors used illustrations of such conditions as Paget's disease and carcinomatosis, and some authors went to the length of stating that Albers-Schönberg's disease was not a rare condition but one which could be produced at will by the ingestion of fluoride.

Flemming Møller showed that the workers in cryolite develop after ten or more years an increased density of the bones—the trabeculae appeared to grow thicker with the deposition of denser material until all their cancellous spaces were obliterated. There was no change in the form of the bones to indicate abnormal osteogenesis or plasticity. Associated with this there was ossification of the tendinous insertions and interosseous fascia. The morbidity and mortality of these affected workers showed little difference from the normal population of Copenhagen (Roholm, 1937). The teeth showed irregularity in opacity and structure; whitish patches were readily detected on examining them.

Paget's disease in the osteoplastic form is never seen throughout the entire skeleton. One side or both sides of the pelvis, one or more vertebrae, perhaps one or more ribs, a part or the whole of the skull, sometimes without changes in the mandible, one or more of the long bones or bones of the hand or foot may show uniform density, all the other bones having a completely normal appearance. Some of the bones may present the appearances described under osteoporosis. Abnormal fragility of the bone which shows the transverse fracture of a stick of chalk may be revealed and this may be followed by the V-shaped extension and osteoporosis. The Paget bone in spite of its density is of increased plasticity; bending and pressure deformities are produced; best seen in the pelvis and the long bones of the lower extremities because the disease at this stage is compatible with normal life.

In the polycythaemias, anæmias and leukaemias of long duration, the bones acquire the so-called osteomyelosclerosis. They become unduly hard and heavy. The cancellous trabeculae are thickened and the interstices filled in with bone. The change in density is not associated with any change in nature or form, i.e. there is no indication of undue plasticity, so that unless of a severe degree, as in the case recorded by Landoff (1944) it may pass unnoticed by the inexperienced observer. It is best seen in radiographs of the pelvis. The changes are uniform throughout the bones, and distinct from fluorosis, there is no concomitant ossification in the tendinous insertions.

Carcinomatosis producing increased density of the affected bones of the skeleton may be seen following carcinoma of the prostate, œsophagus, stomach, &c. These changes are apt to be described erroneously as indicating Paget's disease but they are usually distinctive. In the early stage of development multiple rounded areas of increased density, not very clearly defined, will be seen in the affected bones. These expand and gradually coalesce. The whole pelvis, spine and ribs may show this detail, but the skull and limb bones may show it at this stage only an indication of osteoporosis. This is distinct from Paget's disease in which you may get the pelvis and the whole spine showing the characteristic change but non-uniformity with obliteration of all normal cancellous bone. The whole of the ribs or just isolated ones, and only one or more isolated limb bones may be changed from the normal; further, Paget's disease is a slowly progressive condition in a patient with the deformities due to pressure on plastic bone, whereas the dense bones in carcinomatosis are for they are associated with a very sick patient

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There is a rare and little-known complication of osteogenesis imperfecta which may occur in the adult. It is not only of considerable interest but is important from the diagnostic point of view.

A boy aged 14 in 1937 had had multiple fractures early in life but none for the preceding six years. When 7 the right thigh had been contused, and at 8 thickening of the thigh was noticed. Amputation of the leg had been seriously considered. Radiographs taken in 1937 showed a large amount of open mesh bone surrounding the lower two-thirds of the femur. Now at 24 recent films show the additional bone still present. At 14 there were signs of a fracture of the shaft of the left femur, united with no excess of callus. Ten years later he suddenly complained of pain and swelling of his left thigh. A radiograph five weeks later showed a shadow measuring at least five inches across in the thigh, and its shape and texture suggested the possible presence of a sarcomatous growth. Fortunately we have experience of other cases that have developed similar masses of hyperplastic callus.

Dr. Brailsford, in a paper on osteogenesis imperfecta (1943) referred to four cases complicated by what he took to be subperiosteal hæmorrhages, and he suggested an element of scurvy to account for these. His cases include the one now referred to, copies of the early records and films having been also sent to me by Dr. W. Mackenzie, to whom I am indebted for the recent history and further radiographs.

In 1946 Professor S. L. Baker published a paper on "Hyperplastic callus simulating sarcoma in two cases of fragilitas ossium". We now have records of six other cases (Fairbank and Baker, 1948). Most, but not all, of the eight cases have a background of osteogenesis imperfecta.

The femur is the bone most frequently affected. The hyperplastic callus, with or without a provocative fracture, may, as in this case, extend the whole length of the shaft of the bone. Sometimes the early callus is excessively dense and structureless. Another feature of these cases is the presence of multiple bony excrescences on the shafts of the long bones, particularly along the interosseous borders of the bones of the forearm and leg. Professor Baker has informed me that one of his cases in which, as a result of fractures four years ago, both femora were surrounded throughout their entire length by enormous masses of callus, has also recently flared: at the age of 19 he has developed, quite spontaneously on this occasion, great swelling of one thigh and a new mass of callus. For various reasons we cannot agree with the suggestion of scurvy: histological examination of biopsy specimens in Baker's two cases revealed no sign of old hæmorrhage. Sections showed infiltration of the muscles by œdema and chondroid tissue, while in the deeper layers of the mass there was calcified cartilage and woven bone. Similar histological features were found by Professor Baker after a recent biopsy in Dr. Mackenzie's case. The callus in this case increased still further in thickness and extended the full length of the bone, but now the swelling has begun to subside. It seems highly probable this femur also will remain permanently enlarged. But for the curious behaviour of his two femora, this case seemed to have recovered from his generalized osseous dysplasia.

X-ray films were then shown of an old lady of 73 suffering from osteopetrosis or "marble bones". On admission to hospital (under Dr. Wallace J. Gill) with a minor head injury, the extreme density of the bones and an old fracture of one femoral neck were discovered. Though the generalized osteopetrosis was very severe, there was no anæmia, and no optic neuritis. Spleen not palpable. The

moulding than the normal and for the want of a better term, I have used the term osteoplastic. Generalized osteoplastic change throughout the entire adult skeleton recognizable by radiography, is rare. From time to time one sees a case of Albers-Schönberg's disease in an adult. Such cases are recognized from radiographs taken in the course of investigation of fractures or other conditions. Though the condition may not be recognized until middle or late life it has been present since infancy and would have been detected at an earlier age if radiographs had been taken. In some cases the condition can be recognized in the fetus *in utero*, in others the dystrophic bone commences to be laid down in infancy. As with other general dysplasias and dystrophies of the skeleton it may be so severe as to affect the fetal skeleton seriously and be incompatible with survival; such cases can be detected by radiographs of the pregnant woman. In other cases severity permits of life for a variable period—even to old age—and the dystrophic bone maintains its characters. In the severe degrees of the dystrophy, the dystrophic bone laid down is expanded beyond the normal, giving the long bones club-shaped extremities and the vertebral bodies an expanded denser superior and inferior third. All detail of the structure of the skull may be obliterated so that the radiographs suggest an earthenware skull. In the lesser degrees, and it is these which are discovered accidentally only by radiography, some of the bones may show little departure from the normal shape, though they show little true compact bone and bands of dense bone running parallel to the growth cartilage with little or no evidence of a medulla. Such bones fracture like chalk—the fibrous element being apparently deficient. The nature of the condition may be brought to light because of such a fracture or because of a progressive anaemia or cranial nerve involvement. The radiographic features are distinctive but apparently not generally understood for when Flemming Møller (1934) published his account of the appearances of the bones in fluorosis a number of papers followed on the subject in which the authors used illustrations of such conditions as Paget's disease and carcinomatosis, and some authors went to the length of stating that Albers-Schönberg's disease was not a rare condition but one which could be produced at will by the ingestion of fluoride.

Flemming Møller showed that the workers in cryolite develop after ten or more years an increased density of the bones—the trabeculae appeared to grow thicker with the deposition of denser material until all their cancellous spaces were obliterated. There was no change in the form of the bones to indicate abnormal osteogenesis or plasticity. Associated with this there was ossification of the tendinous insertions and interosseous fascia. The morbidity and mortality of these affected workers showed little difference from the normal population of Copenhagen (Roholm, 1937). The teeth showed irregularity in opacity and structure; whitish patches were readily detected on examining them.

Paget's disease in the osteoplastic form is never seen throughout the entire skeleton. One side or both sides of the pelvis, one or more vertebrae, perhaps one or more ribs, a part or the whole of the skull, sometimes without changes in the mandible, one or more of the long bones or bones of the hand or foot may show uniform density, all the other bones having a completely normal appearance. Some of the bones may present the appearances described under osteoporosis. Abnormal fragility of the bone which shows the transverse fracture of a stick of chalk may be revealed and this may be followed by the V-shaped extension and osteoporosis. The Paget bone in spite of its density is of increased plasticity; bending and pressure deformities are produced; best seen in the pelvis and the long bones of the lower extremities because the disease at this stage is compatible with normal life.

In the polycythæmias, anæmias and leukæmias of long duration, the bones acquire the so-called osteomyelosclerosis. They become unduly hard and heavy. The cancellous trabeculae are thickened and the interstices filled in with bone. The change in density is not associated with any change in nature or form, i.e. there is no indication of undue plasticity, so that unless of a severe degree, as in the case recorded by Landoff (1944) it may pass unnoticed by the inexperienced observer. It is best seen in radiographs of the pelvis. The changes are uniform throughout the bones, and distinct from fluorosis, there is no concomitant ossification in the tendinous insertions.

Carcinomatosis producing increased density of the affected bones of the skeleton may be seen following carcinoma of the prostate, œsophagus, stomach, &c. These changes are apt to be described erroneously as indicating Paget's disease but they are usually distinctive. In the early stage of development multiple rounded areas of increased density, not very clearly defined, will be seen in the affected bone. These expand and gradually coalesce. The whole pelvis, spine and ribs may show this density with obliteration of all normal cancellous detail, but the skull and limb bones may show at this stage only an indication of osteoporosis. This is distinct from Paget's disease in which you may get the pelvis and the whole spine of the ribs or just isolated ones, and only one or showing the characteristic change but not more isolated limb bones may be changed from the normal; further, Paget's disease is a slowly progressive condition in a patient with the deformities due to pressure on plastic bone, whereas the dense bones in carcinomatosis do not usually show pressure deformities for they are associated with a very sick patient.

Section of Ophthalmology

President—HAROLD LEVY, F.R.C.S.

[June 10, 1948]

Anterior Synechia following Perforating Injuries

By P. MCG. MOFFATT, F.R.C.S.

On 20.8.44 the patient, aged 35, was standing in his office on the top floor of the building when a bomb exploded, as he says, about 10 yards away. He finally came to rest in the next room but two, the intervening walls having parted conveniently to allow his transit. He was lowered to the ground on a stretcher by ropes and taken to hospital. On examination, according to report, his general condition was good. His injuries were laceration of the left knee, right forearm, scalp, prolapse of iris of left eye and injury to the lens, cuts in the lower lid, foreign body in the right eye with laceration of the cornea. Immediate treatment consisted of stitching the skin lacerations, abscission of prolapsed uveal tissue and stitching a conjunctival flap over the wound, stitching of the lower lid, removal of the foreign body from the right eye and instillation of atropine and antiseptic drops into both conjunctival sacs. He was transferred to a Base Hospital next day.

He remained at the Base Hospital for nearly seven weeks. The patient states that during that period no operations were performed, but discussions took place regarding an operation for releasing the iris from the wound in the right cornea. It was decided that the eye was too inflamed to allow operative interference.

About 15.9.44 he complained of marked irritation in the right eye, causing a certain amount of pain and watering. This recurred once or twice a week. On October 4 his wife noticed that there was a blister-like swelling over the scar in the cornea. It subsided and on October 7 he left the hospital. During the next five weeks there were repeated "blisters".

January 7, 1945, admitted to the Royal Westminster Ophthalmic Hospital, and the upper two-thirds of the synechia depicted in fig. I (1) were divided on January 8 (2). Two days later the tension in the eye rose but was controlled by eserine and heat until January 12 when the tension rose further and reached its peak on the evening of January 13. It then subsided, possibly as the result of the development of a large blister (3). Thereafter the eye settled down, but blisters occurred at regular intervals and with increasing severity. Short-wave diathermy appeared to cause some improvement, but suddenly in one week he had four large blisters, bigger than any previous ones, lasting four, six, five and eight hours respectively (3). He again entered the R.W.O.H. on March 22 when the scar was treated with iodine and four days later with carbolic, but blisters continued to appear, and the remainder of the synechia was divided on April 3. Rather more than a week elapsed before the blisters appeared (4 and 5), and about this time the patient noticed that he was seeing haloes. The tension measured by Schiötz tonometer was 40 mm. It was decided to decompress the eye, as the sight in this, his only effective eye, was in serious danger. A corneo-scleral trephine

bones of the hands, as usual, showed much less density than the rest of the skeleton. She died at 75. A cross section of the femoral shaft was solid, the medullary cavity having completely disappeared. Microscopic section (Professor W. G. Barnard) showed multiple spherical foci of ossification.

Another similar case died at the age of 63.

In contrast to these, the X-ray film of the hands of another woman, a very mild case of osteopetrosis, shows faint dense transverse bands in the phalanges, and a dense band at the lower end of the femur, the only other part radiographed. There seemed no reason to doubt the diagnosis, since this woman's daughter, aged 6, was unquestionably suffering from osteopetrosis of moderate severity.

Osteopoikilosis or osteopathia condensans disseminata has been seen at all ages from foetal life to over 60 years, and is always discovered by chance, since it produces no symptoms. The dense spots consist of closely packed trabeculae. The appearance of the pelvis with many dense spots, in a man of 24, may be compared with Paget's disease, in which there may be some mottling, but the dense spots are not nearly as discrete as in osteopoikilosis and are mixed with streaks or striations and clear areas, while the surface of the bone is distorted. The skull bones, so commonly showing gross mottling and thickening in Paget's disease, are among the limited number of bones not affected in osteopoikilosis.

Dense mottling of the pelvis may be caused also by metastatic growth from carcinoma of the prostate.

Paget's disease may affect so many bones that it becomes practically generalized.

Hypertrophic osteoarthropathy has resulted from a large number of different affections: it is not always remembered that it may result from an osteogenic sarcoma and this before there is evidence of pulmonary metastases.

A young woman of 19 had had a leg amputated three years before for a spindle-celled sarcoma, with much calcification in it, growing from the tibia. Well-marked signs of generalized osteoarthropathy and clubbing of the fingers. Large secondary retroperitoneal growth but no signs, clinical or radiographic, of metastases in the chest. Subperiosteal shadows were seen on the shafts of all the long bones. Two months later she died and at autopsy secondary growths were found in the lungs. Another similar case, a young man with an osteogenic sarcoma of the lower end of the radius, was treated by amputation. In the following nine months before he died he developed well-marked changes typical of osteoarthropathy.

Endocrine errors.—Most of the epiphyses were still ununited in one case (radiographs shown)—that of an intelligent perfectly proportioned dwarf of 46. His height was 4 feet; his voice high-pitched. The condition was regarded as due to hypopituitarism as the radiographs of the skull show a calcified cyst of the pituitary with enlargement of the pituitary fossa. (By courtesy of Mr. St. J. D. Buxton.)

With regard to thyrotoxic osteoporosis I can remember seeing only one case in which the osteoporosis was severe enough to result in more or less spontaneous fractures.

In senile osteoporosis the spine seems to suffer much more than the rest of the skeleton. Multiple collapse or crushes of the vertebral bodies are, of course, common. After a period of recumbency, preferably in a plaster shell when the pain is sufficiently severe, one likes to make use of some form of spinal jacket or brace. My experience, however, has been that many of these old ladies refuse to put up with a brace and prefer to suffer a certain amount of discomfort. In many such cases the ordering of a brace means wasting their money.

I would like to refer briefly to:

One case with multiple pseudo-fractures (Milkman's syndrome) since the sex of the patient is unusual. A man of 34, a miner, had broken his right leg (tibia and fibula) five years before. Union did not take place and a bone-grafting operation was necessary. He had not walked for the past four years. A year ago his neck had been explored but no parathyroid tumour was found. Biochemical investigations revealed nothing abnormal. Radiographic examination showed many typical pseudo-fractures and some general osteoporosis but the latter was not very marked.

Was the condition of this man simply due to prolonged inactivity? Owing to the war the later history of the case is unknown.

Lastly a point mentioned by Snapper (1943) is worthy of attention.

When multiple cyst-like lesions are present in the bones and the diagnosis of xanthomatosis versus fibrocystic changes is under consideration, he strongly advises the selection of a small young lesion for biopsy. He points out the typical cells of xanthoma are associated with a good deal of fibrosis in the lipid granulomatous tissue, and in an old lesion the xanthoma cells may have disappeared completely, leaving nothing but fibrous tissue. This he maintains has often led to an erroneous diagnosis.

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Section of Ophthalmology

President—HAROLD LEVY, F.R.C.S.

[June 10, 1948]

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By P. MCG. MOFFATT, F.R.C.S.

ON 20.8.44 the patient, aged 35, was standing in his office on the top floor of the building when a bomb exploded, as he says, about 10 yards away. He finally came to rest in the next room but two, the intervening walls having parted conveniently to allow his transit. He was lowered to the ground on a stretcher by ropes and taken to hospital. On examination, according to report, his general condition was good. His injuries were laceration of the left knee, right forearm, scalp, prolapse of iris of left eye and injury to the lens, cuts in the lower lid, foreign body in the right eye with laceration of the cornea. Immediate treatment consisted of stitching the skin lacerations, abscission of prolapsed uveal tissue and stitching a conjunctival flap over the wound, stitching of the lower lid, removal of the foreign body from the right eye and instillation of atropine and antiseptic drops into both conjunctival sacs. He was transferred to a Base Hospital next day.

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About 15.9.44 he complained of marked irritation in the right eye, causing a certain amount of pain and watering. This recurred once or twice a week. On October 4 his wife noticed that there was a blister-like swelling over the scar in the cornea. It subsided and on October 7 he left the hospital. During the next five weeks there were repeated "blisters".

January 7, 1945, admitted to the Royal Westminster Ophthalmic Hospital, and the upper two-thirds of the synechia depicted in fig. I (1) were divided on January 8 (2). Two days later the tension in the eye rose but was controlled by eserine and heat until January 12 when the tension rose further and reached its peak on the evening of January 13. It then subsided, possibly as the result of the development of a large blister (3). Thereafter the eye settled down, but blisters occurred at regular intervals and with increasing severity. Short-wave diathermy appeared to cause some improvement, but suddenly in one week he had four large blisters, bigger than any previous ones, lasting four, six, five and eight hours respectively (3). He again entered the R.W.O.H. on March 22 when the scar was treated with iodine and four days later with carbolic, but blisters continued to appear, and the remainder of the synechia was divided on April 3. Rather more than a week elapsed before the blisters appeared (4 and 5), and about this time the patient noticed that he was seeing haloes. The tension measured by Schiötz tonometer was 40 mm. It was decided to decompress the eye, as the sight in this, his only effective eye, was in serious danger. A corneo-scleral trephine

(6) was performed on April 12. Recovery was uneventful and from that time he has never had another blister.

The best vision before the operation was 6/18 with -5.0 D.S., $+7.0$ D.Cyl Ax 60° , but one month after the vision had improved to 6/9 with -1.25 D.S., $+3.0$ D.Cyl Ax 65° .

He returned to work and was without complaint in this eye until February 1946 when he suddenly noticed haloes. The tension was 45 mm. and the trephine was filtering poorly. The operation was repeated a little to the outer side of the first (7) on March 14. Convalescence was uneventful and since then he has had no further trouble. The vision when last recorded on June 9, 1948, was 6/5 with -4.0 D.S., $+2.5$ D.Cyl Ax 65° . The trephine

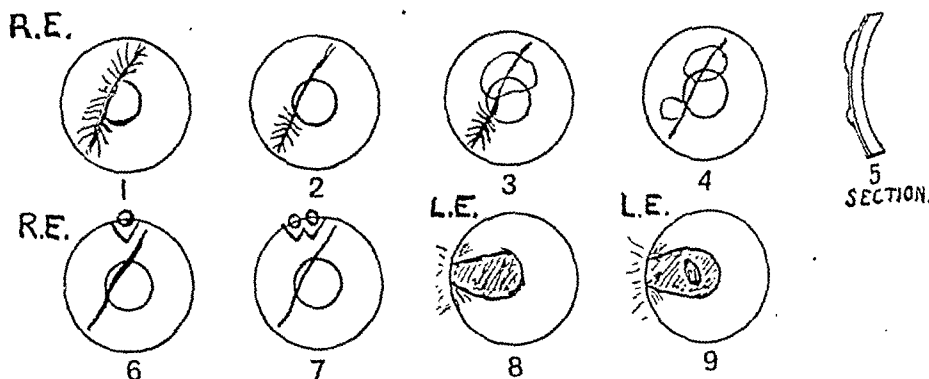


FIG. I (1 to 9).—Flying bomb injuries, 20.8.44.

was filtering well, the tension normal, the field of vision to $\frac{1}{4}^\circ$ white test object almost full, but there was slight enlargement of the blind spot. The disc is a little pale and shows some pathological cupping. He experiences no handicap except when driving a car at night.

The left eye (8 and 9) was never a source of physical discomfort and gradually settled, some of the lens matter absorbing after some months. The eye was always regarded as a doubtful asset although the projection was accurate. There was a history of hypotonia for some weeks after the injury. However it was felt that no harm would be done by attempting to make a hole through the remains of the lens, and it would increase the field of vision on the left side and possibly provide a useful spare part should anything happen to the right eye. The result was rather disappointing because, although a small gap was achieved (9) through which the fundus can be seen, changes at the macula and in the lower half of retina were found. The best vision is 3/60 with correction and there is loss of the upper portion of the field of vision.

So far as the right eye is concerned, I think the chief factor in the development of the glaucoma was probably delayed formation of the anterior chamber. It is probable with a wound of this size which was uncovered, that leakage of aqueous was considerable and there had been time for peripheral synechiae to form. Whether this could have been avoided by covering the wound by a conjunctival flap at the earliest opportunity is a matter for speculation, but it would seem to be rational treatment in such cases. An alternative explanation might be that the anterior synechiae caused a rise in tension by mechanical and reflex irritation of the ciliary body with increased output of aqueous in the first place, and later on the development of peripheral anterior synechiae and gradual occlusion of the filtration angle. If so, the early division of the synechia might have prevented the onset of secondary glaucoma. It is, however, easy to understand the reluctance to do this in an only eye which was inflamed. The final choice of trephining as the most suitable operation for decompressing the eye was made on the assumption that a permanent filtering scar was necessary, and this operation was the one that gave the best consistent results.

The full significance of the blisters was not realized until the patient began to complain of haloes. Except for the attack of acute glaucoma following the first operation for division of the synechia, the tension was thought to have been normal. The scar appeared to be well healed although there were particles of pigment incarcerated in it, and it was difficult to believe that such a scar could be leaking. I think that the resistance of the scar to the passage of aqueous was overcome from time to time when the tension rose above a certain level and blisters formed. At any rate no more blisters occurred after the eye was decompressed. Fluorescein did not give any useful information.

The following is a brief account of 12 cases of anterior synechiæ following perforating injuries which have come my way.

The first group (fig. II) consists of four cases which did not have any injury to the lens.

- (1) An injury with glass in which the iris was not prolapsed, but was caught in the wound. The iris was separated from the scar about a week after the injury and no complications ensued.
- (2) An injury with a pebble in which the iris was incarcerated in the wound. Mydrine was injected subconjunctivally but the anterior chamber was not formed twenty-four hours later so a conjunctival flap was sewn over. The iris was not free. The A.C. formed on the fifth day. Subsequently four attempts were made to divide the synechia with Lang's twin knives. The A.C. was lost on each occasion and there still remains a fine thread adhering to the scar. The tension is normal but the vision is only 6/36 due to retinal changes.
- (3) Slice with a chisel. Prolapse of iris was abscised and the cornea was covered by a purse-string conjunctival flap. Synechiæ were present at each end of the scar. These were divided by Lang's twin knives within eight weeks of the injury. There were no complications.
- (4) Puncture wound with a fine wire. This patient attended Mr. Gayer Morgan's outpatient department at Guy's Hospital when I was Registrar. There was a history of injury some weeks before which was regarded as trivial. The symptoms were pain in the eye and misty vision. The tension was raised, the cornea steamy and a fine adhesion existed between a punctate scar and the surface of the iris. The synechia was divided by a knife needle and the symptoms subsided. There was no further trouble.

The second group (fig. II) comprises 4 cases in whom there was no injury to the lens but who had had a complete iridectomy. In this group glaucoma was not likely to develop. (1) An intraocular foreign body had been removed by magnet and a complete iridectomy performed at the same time. There were symptoms of irritation, photophobia and pain. A fine synechia

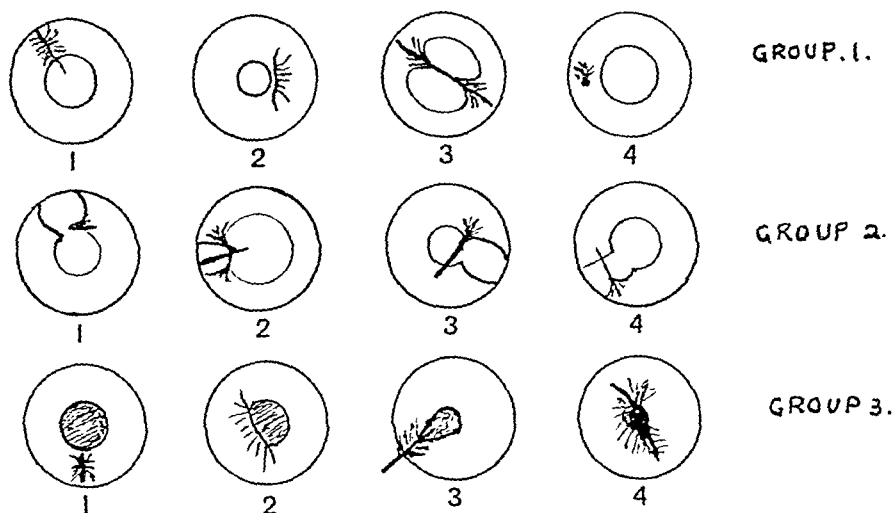


FIG. II (Groups 1, 2, 3).—Anterior synechiæ following various types of perforating injuries.

stretched from the wound of entry of the foreign body and one pillar of the coloboma. This was divided by a knife needle and the symptoms were relieved. (2) Injury with glass from a broken door. Prolapsed iris was abscised and the wound covered by a hood of conjunctiva. Synechiæ extended from the edges of the coloboma in the iris to the corneal scar. There were symptoms of irritation, aching of the eye and photophobia. At operation it was possible to divide only the synechia between the lower pillar of the coloboma and the scar. The symptoms persisted to some extent until the upper synechia was divided. (3) Motor accident in which a corneal injury occurred due possibly to flying glass. (4) Slice with a chisel. Both cases had a fine adhesion between one pillar of the coloboma and the scar left after abscission of prolapsed iris. There were no symptoms of irritation so the synechiæ were not divided.

The third group (fig. II) consists of cases in which the lens had been damaged at the time of the injury. (1) Perforation with a spicule of metal which the patient had removed himself. A

small synechia was attached to the scar in the cornea. There was a stellate opacity in the posterior cortex of the lens. The synechia was divided by knife needle without losing the anterior chamber. The lens opacity continued to spread and it was intended to remove the cataract but the patient ceased to attend the hospital. (2) Injury with a piece of concrete. Wound was covered by a purse-string conjunctival flap, after abscission of prolapsed iris. The lens gradually absorbed, but there was an extensive adhesion of iris to the back of the corneal scar. This was divided completely and the eye has remained quiet ever since. (3) Injury with a piece of broken spectacle lens. The wound involved cornea and sclera. This was covered by a conjunctival flap. The iris became firmly attached to the scar. The lens partly absorbed. Fine "K.P." appeared but the eye settled down after some weeks. Division of the synechia was attempted after about eighteen months but hyphæma developed and the tension rose. As the blood absorbed the tension came down and the eye became quiet. Projection of light was found to be very defective and it was decided to do nothing further. (4) Injury with a stick which had produced a large-stellate wound in the cornea. Prolapsed iris was abscised and the wound covered by a purse-string conjunctival flap. The eye settled down but extensive adhesions between the iris and the scar remained. The lens appeared to be absorbing satisfactorily, when the patient was evacuated to the country. He was not seen again for over a year and then was found to have the iris knotted to the centre of the scar. The eye, which was blind, painful and hard, was excised.

The following comment is tentative only:

Where there is a corneal wound, unless it be small, it should be covered by a conjunctival flap, care being taken that it does not exert undue pressure on the cornea. Not only does it prevent infection from entering the eye, but it promotes closure of the wound, favours anterior formation of the anterior chamber, and lessens the likelihood of peripheral synechia. Anterior synechia should, as a rule, be divided because of the risks of secondary glaucoma arising later. If a complete iridectomy has been done, this risk is probably much less. Professor Goldman of Berne states that the tension does not begin to rise until 270 degrees of the circumference of the filtration angle have been occluded, so it would seem that other factors are involved in the production of secondary glaucoma in some of these cases.

The presence of anterior synechia does appear to be a cause of symptoms which may be disabling to the patient, and division of the synechia is indicated.

Unfortunately no gonioscope was available for examining the cases, but it is hoped that this will be remedied in the near future and more complete observation will then be possible.

Mr. H. Neame said that anterior synechia were sometimes very difficult to separate, particularly the long linear type. With regard to the occlusion of 270 degrees, three-quarters of the circumference, surely there must be variation with the age of the patient. He had seen middle-aged or elderly people who had had a relatively small anterior synechia after injury develop glaucoma fairly soon. Admittedly, one had not examined them with the gonioscope, but young people with extensive synechia did not develop glaucoma, though he had always felt doubtful as to whether it was wise to leave them alone, because of the possibility of their developing glaucoma in twenty or thirty years' time as a result of the reduced angle of the anterior chamber. He could not accept Professor Goldman's statement—as quoted by Mr. Moffatt—without some corollary as to the age of the patient.

Mr. M. H. Whiting thought that the possibility of dealing with penetrating wounds by a corneal suture might be considered. In the *British Journal of Ophthalmology* some months ago there was a description of the anatomical results obtained by the use of a conjunctival flap, and the writer showed how inaccurate the apposition of the corneal surface usually was in such a case (Levykoieva, E. Th., 1947, *Brit. J. Ophthalm.*, 31, 336). There was no reason why with sutures one should not get apposition as accurately as in suturing wounds in the skin.

Anterior synechia should be divided as early as possible, and if the eye happened to be inflamed that was an indication for dealing with the synechia without delay. There were various methods of dealing with anterior synechia following perforating injuries; probably the most difficult were those which were close in to the angle. In Case 3 of the last series described by Mr. Moffatt there was an example of synechia with which the speaker had found it useful to deal by making a broad needle incision on either side of the synechia and pulling the iris out with an iris hook and then cutting it through so that the synechia were not actually removed but successfully isolated from the rest of the eye.

Mr. Whiting agreed with Mr. Neame that to talk of 270 degrees of synechia being necessary in order to produce glaucoma was nonsense. It was not merely the anatomical condition of the angle; it was the fact that the iris was continually contracting and dilating, and the pupil doing likewise, so that there was a constant irritation to the eye from the adhesion of a portion of the iris, which ought to be mobile, fixing it. That had a considerable effect not only on the irritation but also on the rise of intraocular pressure.

Dr. N. Pines contended that for the formation of an anterior synechia three conditions were necessary: the wound in the cornea must have the membrane of Descemet turned in such a way that it could not be reconstructed so that the endothelium would commence to proliferate. Secondly, the wounding of the iris was done in such a way that the epithelium of the iris was injured and commenced to proliferate. A third and consequently important factor was the delayed formation of the anterior chamber. This was why it was necessary to follow the original idea of Kuhn and to apply, in the first place, scleral or corneal stitches in the gaping wound of the cornea. A conjunctival flap in itself did not bring the edges of the wound together. Secondary glaucoma, according to Levkoieva, was formed by proliferation of the endothelium of the cornea or the epithelium of the eyes or both of them forming a thin line across the corner of the anterior chamber.

Dr. Pines submitted that Mr. Whiting was right in saying that synechiæ should be dealt with as early as possible. He had just reviewed a book on the subject from Russia in which it was emphasized that to avoid complications it was well to suture the cornea as early as possible so as to prevent any proliferation.

Mr. A. S. Philips said that, besides allowing re-formation of the anterior chamber, if the suture was used it also allowed the surgeon to inspect the anterior chamber day by day to see what was going on inside. That was impossible when there was a conjunctival flap.

With regard to Lang's twin knives, clearly if the anterior synechia was to be divided successfully it was essential not to lose the anterior chamber, and that could only be achieved if Lang's twin knives were exactly a twin set; the area of the cross-section of the shaft of the two instruments should be identical. Often they became transposed and the only way to check whether one had a true twin set was to use a gauge. Unless the knives were a pair it was safer not to use the second Lang's twin knife but to do the whole operation with the first. That did just as well because the side of the perforating instrument was also sharp and would cut the synechiæ as well as did the cutting instrument.

Mr. F. W. Law said he had hitherto believed that the essential part of the twin knives was that the blunt one was fatter than the sharp one. Therefore was Mr. Philips right on this important point?

Mr. Affleck Greeves put in a plea for complete anaesthesia, either local or general, before division of an anterior synechia was performed. In his experience if anaesthesia was complete and great care taken and proper time given to the operation, then one instrument was all that was necessary. It was all-important that as far as possible no aqueous should be lost.

The President did not think the value of corneal suture in such injuries had been appreciated to the full extent. It was not difficult to do. Good apposition of the wound edges could be obtained, and a flap became unnecessary. In any case, there were always cases that gave rise to anxiety.

Mr. Moffatt thanked Mr. Whiting for his description of a method of isolating a peripheral synechia, a method of which he had not hitherto thought. He had, however, thought of using a keratome to divide the synechia.

Mr. Moffatt had not, so far, sutured any of the perforating wounds because of the risk of increasing the damage already done.

With regard to Dr. Pines' remarks as to proliferation of epithelium, it might be that when members became more familiar with the gonioscope they would be able to see how much peripheral anterior synechiæ actually existed in cases which developed glaucoma, or even in those which had not developed glaucoma but had had a synechia for some considerable time.

Mr. Neame had queried the correctness of Professor Goldman's statement as to 270 degrees. Mr. Moffatt had gathered that Professor Goldman had been taking that figure as the amount of peripheral anterior synechiæ, excluding other complications, required to produce glaucoma.

Mr. Moffatt added that he had not said very much in regard to the methods he had used for division of anterior synechiæ. He mostly used the Lang's twin knives, sometimes he used the sharp pointed knife only or a knife needle. He believed that a stout synechia could be more easily divided with a Graefe knife though he had always been afraid he might damage the cornea in the attempt.

Mr. Moffatt agreed with Mr. Greeves that complete anaesthesia was essential; certainly in the case of young people he personally had always had them under a general anaesthetic before attempting to divide the synechia.

Mr. Philips, in reply to Mr. Law, said that he thought that Lang's twin knives were made not with a constant uniform shaft but that the shaft became thicker as the handle was reached. The perforating needle, the first one, was only just put inside the anterior chamber and so the narrow section of the shaft was engaged, the following knife was pushed through into the anterior chamber, so that as the shaft became much thicker, the thicker portion of the shaft engaged in the hole.

Exfoliation of the Lens Capsule in Each Eye.—P. MCG. MOFFATT, F.R.C.S.

W. A. H., aged 52. Has spent most of his life in India. Shortsighted from boyhood. Five years ago he noticed blurring of vision and coloured haloes round naked lights. He has been examined many times under suspicion of glaucoma, but the Schiötz measurements have always been within normal limits, and the fields of vision show no deterioration.

R.V. 6/18 with -5.5 D.S.

L.V. 6/18 with -4.5 D.S., -1.0 D.Cyl. Ax 180° .

Examination shows exfoliation of the lens capsule, particles floating in the anterior chamber and frost-like deposits on the margin of the pupil and elsewhere.

Mr. F. A. Williamson-Noble thought Mr. Moffatt would remember that when they were in Switzerland together and Professor Goldman demonstrated the use of the gonioscope he had said it was possible when using the instrument to see flakes lying in the region of the angle and that these flakes gave rise to the glaucoma. Could that apply to the exfoliation under discussion?

Mr. H. Neame asked if any member had any knowledge of what happened to those with exfoliation of lens capsule if they were operated on for glaucoma. Did the drainage become obstructed again? He presumed it would be no use to wash out the anterior chamber because that washing-out would have to be repeated several times. Had any member watched such cases following operation for glaucoma?

Mr. Moffatt said there had been a paper on the subject (Gradle, H. S., and Sugar, H. S., 1947, *Amer. J. Ophthal.*, 30, 12); and the point as to operation for glaucoma had been mentioned "... Since there is a tendency for the drainage path to be closed by further exfoliated shreds carried there from the lens surface by the newly diverted current of the aqueous, any glaucoma operation must be followed by the constant use of miotics to prevent further exfoliation from the capsule..." Removing the lens did not relieve the glaucoma if it was already present. Gradle and Sugar had reviewed 77 cases in their paper.

Section of Dermatology

President—J. E. M. WIGLEY, F.R.C.P.

[April 15, 1948]

Modern Conceptions Concerning the Compulsory Isolation of Lepers

Contagious Malignant Morbus Hansen versus Non-contagious Benign Hansenide

By R. D. G. PH. SIMONS, M.D.

*Privat docent at the University of Leiden
Dermatologist of the Civilian Hospital Amsterdam*

It is deplorable that even to-day some dermatoses may be diagnosed as leprosy, thus leading to wrong and inadequate treatment. The patient too, may abandon all medical care in fear of compulsory isolation as a leper.

Syphilis and leprosy are often confused. Because the Wassermann test may sometimes be positive in leprosy it may also happen that syphilis is not diagnosed in a leper. This unfortunate occurrence (which only happens in rare forms of malignant leprosy) has been the cause of the erroneous opinion that a positive Wassermann reaction is only a freak of leprosy, instead of the coincidence of syphilis being suspected *a priori*.

The classification of leprosy is highly important.

There is one point, however, which invariably appears in all classifications, even in that of the Second Pan-American Conference of Leprosy in 1946¹, namely that there is a non-contagious and benign form of leprosy.

Morrow in 1854 and Stelwaggon in 1910 divided leprosy into two groups: (1) *Lepra tuberosa*; (2) *lepra maculo-anæsthetica* or *lepra nervorum*.

In 1931, at the Congress of Manila, a new division was made: (a) Neural leprosy; (b) cutaneous leprosy.

This classification, however, was misleading, as "neural" did not imply neurological, and "cutaneous" did not exclude an involvement of the nerves. The latest international classification was made in Cairo in 1938, and it is still in official use. It divided leprosy into two main groups: (a) Lepromatous leprosy (L) which is leprosy of the skin, nerves, glands and internal organs; (b) Neural leprosy (N) which corresponds approximately to the former maculo-anæsthetic leprosy.

The meaning of both terms has more or less altered with the advance of time. Nowadays lepromatous leprosy (L) implies the multibacillary, malignant, and contagious type, whereas neural leprosy (N) implies a paucibacillary, non-progressive, benign and non-contagious form. The so-called lepromine test is negative in the former (L) and positive in the latter (N), because of the abundance of antibodies. The (N) leprosy is again subdivided into Na, mainly anæsthetic, Ns the more visible form and Nt, the tuberculoid form. The Havana Congress, 1948, classified leprosy as lepromatous, tuberculoid and indeterminate (not intermediate) leprosy.

Another very important factor in classification is Virchow's globus or leper cell. This consists of a great number of vacuoles ("foam cell") containing a fat or lipid, as well as a multitude of leprosy bacilli. In those cases where leprosy bacilli are seen in "cigar bunches", one can assume the presence of a rudimentary globus. Leper cells or "cigar bunches" are characteristic of lepromatous leprosy, they are absent in N-leprosy.

This is an important point, as the nose has been regarded as the "porte d'entrée" of leprosy, or the positive nose-smear as the first symptom. However, in the majority of lepers (nearly all N-leprosy) the discharge from the nose is negative. A positive nose-smear, therefore, is not an initial symptom of leprosy, but a symptom of degree, since it indicates

¹This is not the international conference. The international Cairo classification is still the official one. In the Havana Congress (1948) the same opinion was expressed.

malignant lepromatous leprosy. A positive nose-smear generally only contains "cigar-bunches" thus indicating leprosy L. Just as in tertiary syphilis, lepromatous leprosy has a predilection for the nose.

A transformation of N into L leprosy (compare the transformation of a tuberculide into lupus vulgaris) is very rare (Schujman, Rodriguez, Plantilla and Wade). In fact, N and L leprosy should be regarded as "polar forms", separated from each other by a "no man's land" in which a true transmission from N into L leprosy is most improbable (Cochrane).

A diagnosis of the different types of leprosy is a difficult task and calls for specialized knowledge. For instance the infiltrative process in N-leprosy can be so pronounced that induration can be felt and N-leprosy seems to simulate L-leprosy (Davey), which is also infiltrative. When a similar picture of tuberculoid is found in tuberculosis, it is called "sarcoid".

Thus tuberculoid leprosy (a histological concept), will rarely be tubercous (a clinical or morphological concept), though tubercous leprosy usually implies the malignant lepromatous leprosy, whilst tuberculoid leprosy (also called lepride) implies the most benign leprosy.

Rogers, who traced the source of infection of his patients, found that 94.7% of it was due to L-leprosy. In the remaining 5.3% a new infection was traced to contact with a nerve case; probably a mixed type with preponderance of nerve symptoms.

To summarize, there are two main types of leprosy: (1) The contagious malignant form. (2) The non-contagious benign form.

It should therefore be quite possible to find a terminological solution, which according to my mind lies in the *name* of the disease.

If, however, the misleading habit of calling all types of leprosy Morbus Hansen should persist, it will be a definite regression and we shall labour under the same misapprehensions and difficulties as our colleagues in the Middle Ages. We shall class the lepride with leprosy or Morbus Hansen and thus condemn 80% of those suffering from the benign type of the disease with the 20% suffering from malignant leprosy.

It is not generally realized that the majority of patients formerly called lepers are not leprosy in the old sense of the word, but suffer from a benign disease. Their segregation is unscientific, unreasonable and inhuman: "The whole weight of modern, competent opinion is that such cases (i.e. 80% of all (Rogers)) are no danger to the public and that their segregation only encourages false and misleading fear" (Brit. Emp. Lep. Relief Assoc.).

The new term "Hansen's disease" has been explained in a non-medical magazine, thus instructing the public as to its real meaning. That is another reason for separating the benign form from the Hansen terminology.

In the case of treponematoses a similar incidence arose accidentally. Yaws and syphilis are caused by spirochetes which cannot be differentiated, though nobody will ever mistake the one disease for the other. And so to my point: just as some benign forms of tuberculosis, i.e. Boeck's sarcoid and Bazin's erythema are called *tuberculide*, so should the term Morbus Hansen or leprosy be differentiated from the term Hansenide. This new terminology should give the N or T patients a new lease of life and the *ghastly alternatives of either no medical treatment or barbed wire for life would no longer confront them*.

Muir and Rogers therefore suggest using the term "neuritis" in such cases, "thus excluding difficulties due to unreasoning prejudice". In Surinam such cases are called "suspect".

If, therefore, such Hansenide patients are still in leper homes, they should (provided a well-established diagnosis is made) immediately be released, sent home or to a sanatorium for treatment. Treatment should be mainly directed towards a general improvement of health and increase in resistance. Too active treatment should be avoided.

Much money will be saved this way, which in turn "can be well devoted in increasing the attraction and treatment in leper homes for the *infective* cases" (B.E.L.R.A.).

As to the contagiousness of leprosy: The origin of infection is still open to argument. Many people in fact claim to have demonstrated a direct contact infection, whereas others insist on having found an inanimate medium.

Hundadze, Pefard, Mitchell, Marchoux, Ehlers and others, have described cases in which physicians were contaminated following an injury during treatment of a leper. Blanchard, Blanquier, Mitsuda, Kensuke, &c., described incidents of leprosy primarily due to the custom of tattooing. Hildebrandt tells of a child which had infected itself by pricking its skin with a needle with which another child had demonstrated the analgesia of its leprosy skin. Strain found the beginning of leprosy in the wound of a breast excision in a woman, whose son had been suffering for three years from manifest leprosy. De Lange reviews an infection from a morphine syringe. Infection by clothes has been described by Arning, Looft, Romer, Hansen, Lorand, and many others. Bergmann observed that 20% of female hobsies working in leper colonies sooner or later acquire the disease. Broers van Dort, Gougerot, Giordano, Muir and Simons among others described the origin of infection,

or probable infection from soil, i.e. from walking with bare feet. It is a well-known fact that the slightest injury of the leprous skin of a lepromatous leper exudes bacilli. This in turn finds its practical use in the examination of the serum from leprous earlobes.

Leprous bacilli may be present in all layers of the skin, but it is by no means certain that normal scaling of the skin does expose bacilli. According to des Essarts, bacilli in the hair follicles may "grow out" with the hair and furthermore bacilli from the sweat glands may be brought to the surface by the action of these glands.

It is, however, still questionable whether the infection is due to direct or indirect (intermediary) contact. What is certain is the fact, that the disease is epidemic in some areas, and it is practically certain the "contact" (direct or indirect) for infection must be close and of long duration. The disease is not only confined to certain countries, but is, in fact, found in particular areas, or even particular houses. Should there exist an intermediary factor, such as an insect, it is bound to have a short "action radius".

Since the disease is neither waterborne (occurring in towns and villages along rivers), nor airborne (occurring in disseminated areas due to mosquitoes and the like), it must be assumed that it is, like scabies, a "familial disease".

As infection usually only occurs after long-continued intimate contact with the source, I am of the opinion that the disease is not highly contagious and that the risk of infection is relatively small, though one should never be exposed to this small risk for any length of time.

Moiser found acid-fast bacilli, similar to those of leprosy, in 69% of cockroaches from leper colonies. Although it is possible that these bacilli may also exist in cockroaches that do not come from leper homes, it is an important feature, which requires serious hygienic measures.

An even more likely carrier of infection is the common bed bug, particularly as it is, in contrast to cockroaches, a blood-sucking insect. Goodhue, Ehlers, Bourret, Sandes, Lebœuf, Skelton, Perham, Thomson, Johnston, Da Buen and many others (Rogers) have detected acid-fast bacilli, similar to leprosy bacilli, in bed bugs.

But quite apart from the *mode* of infection, one can assume from all investigations that L-leprosy is infectious. The danger of infection should neither be exaggerated nor underestimated.

Rogers, Muir, Cochrane and others claim that children are particularly prone to infection. Manalang goes so far as to state that only children can be infected, whereas adults are immune. Children are usually taken early from leprous environments, and, should they happen to be born in it, they are removed as soon as possible.

Of great value for the demonstration of the epidemiology of L-leprosy and the non-infectiousness of N-leprosy is the so-called *Nauru epidemic*. In 1912, a leper woman from the Gilbert Islands was allowed to enter Nauru, a Pacific (South Sea) Island. This happened against the advice of the quarantine physician. In 1925, 368 new cases, i.e. one-third of the whole of the population, were found to be infected: an infection which could be traced to this one case. In spite of the panic caused by this epidemic, Rogers, in fighting it, advised the isolation of only the 189 L cases. A decrease of infected cases was noticeable in 1933, and in 1937 there remained only 57 L and 102 N cases. "Thus one of the most serious epidemics in history had been got under control" (Rogers). (Unfortunately no further developments can be reported, as the Japanese drowned all surviving patients during the occupation.)

The dangers of compulsory measures are the following: patients dare not report the disease. This not only leads to wrong statistics, but in addition patients cannot be treated and hidden cases form a great potential unchecked danger. Still worse, thousands of people suffering from diseases wrongly regarded as leprosy do not report for medical treatment.

"Total segregation therefore spreads leprosy" (B.E.L.R.A.).

"Where it becomes known that patients are to be shut up for life, lepers will conceal themselves outside and keep on—those are the L cases—spreading the disease" (B.E.L.R.A.).

When a house-to-house investigation was carried out in India, it became evident that for 102,000 known cases, over one million were hidden, of which one-quarter were of contagious type. Only 14,000 cases are isolated, of which 5,000 are non-contagious (Rogers).

In 1925, the South African Government ordered an examination of 3,501 patients who were "immured in prison-like asylums"; 800 were found to be non-contagious and were released. The result was striking; from that moment twice as many cases (about 4,000) reported voluntarily. Of a total of 6,769 cases, 60% (4,052) could be released again after having received adequate treatment. 61% remained free of any symptoms for the next five years. For this reason nobody to-day will advise the obsolete method of "hunting down hidden lepers like wild beasts" (Rodriguez).

"Millions have been spent on segregation, without any effective good and millions more will be wasted on it" (Moiser).

"Segregation is a regrettable necessity in the case of infective lepers. But we have no right on humanitarian grounds to separate a man from his wife and family, unless there are adequate public grounds for doing so" (B.E.L.R.A.).

Hansenide—i.e. N-leprosy—patients should not be isolated.

"It is therefore imperative that the line of demarcation as far as segregation is concerned, should rest not on the diagnosis of leprosy but on the differential diagnosis between the infectious and non-infectious leper!" (Rogers and Muir.)

"Let us change our methods: We know that compulsory segregation has proved worse than useless" (Moiser).

"The whole concept of total segregation is out of date" (B.E.L.R.A.).

Conclusions.—"As long as we had no treatment of material value there was some excuse for recourse to the crudities of the Middle Ages: lifelong segregation of lepers" (Rogers and Muir). To-day, however, there remains no doubt that one can save energy and money by isolating only the malignant lepromatous and not the Hansenide patients.

The Hansenide patients who leave leper colonies, will in their turn encourage others to undergo adequate treatment, since they will see by this example that leprosy is no longer a crime for which the only punishment is imprisonment for life, but that it is curable and certainly in two-thirds of all cases not even contagious. Lepers and sufferers from disease classified as leprosy will no longer fly from the police and . . . the doctor!

The answer to the question what should be done with the isolated patients is twofold.

(a) All patients with L-leprosy should remain in isolation. Leper homes should be called "clinic" or some such name. Diagnosis should be negative for at least two years without the appearance of new symptoms before the patient's discharge is considered. This period of two years has been decided upon, as any shorter interval has resulted in too many relapses (Culion).

(b) All Hansenide patients (N or tuberculoid leprosy) should be discharged immediately, though they would have to remain under regular supervision of a skin specialist.

The following should be cared for by the public health authorities: Those Hansenide patients who suffer from general poor health, or who return to unhealthy and poor environment, also patients who are likely to turn to prostitution or to contract tuberculosis—24% to 32% of all lepers die from tuberculosis and many more suffer from it (Faget).

In conclusion I would say again that segregation should depend not on the diagnosis of leprosy, but on the differential diagnosis between infectious malignant leprosy and the non-infectious Hansenide.

Schamberg's Disease.—H. W. BARBER, F.R.C.P.

Miss I. W., aged 62.

History.—In December 1944, she stated that she had been subject to attacks of *follicular tonsillitis* all her life, and that at the age of 18 she had a particularly severe one which was followed by *chorea*. Although there is no valvular disease of the heart, she had at one time frequent extrasystoles, but these diminished, and a report by Dr. Peter Miles (19.7.39) on her cardiovascular system revealed no organic changes, only occasional extrasystoles.

The eruption appeared first in August 1944 on the inner side of the left knee. Later the anterior surfaces of the legs and the skin between the toes became affected. The eruption continued to spread, eventually involving the legs, particularly over the knees, the elbows and forearms, the palms and soles and the skin between the fingers and toes. Patches also appeared on the abdomen, shoulders, and inner thighs.

The tonsils were clearly infected, and she was admitted to Guy's Hospital in August 1945 for their removal; afterwards she was given a five-day course of sulphamezathine, during which there was an exacerbation of the eruption. This was followed by a general subsidence.

December 14, 1945: The eruption was still present on the legs, over the patellæ and elbows, and on the forearms and palms, but was much less active. Small new patches appeared from time to time. She continued, however, to have sore throats, particularly in the left tonsillar fossa, where periodically a remaining portion of lymphoid tissue became inflamed and ulcerated.

In July 1946 there was an exacerbation on the hands and wrists and in August 1946 she was again admitted. An ulcer in the left tonsillar fossa was present, but cultures from this revealed only *Streptococcus viridans* and no B-hæmolytic strains.

Summary of investigations by Dr. R. L. Waterfield: Slightly raised B.S.R.; slight simple anæmia with slight lymphocytosis. Blood clotting time was normal.

Intramuscular injections of penicillin—300,000 units twice daily for ten days—were given and she was then discharged.

From then onwards the active eruption has gradually disappeared, and there has been great improvement in her general health. Occasionally, however, there have been recurrences of the inflammation with ulceration in the remaining portion of infected lymphoid tissue in the left tonsillar fossa. When this occurs she feels unwell and *new active lesions always appear on the left forefinger.*

When last seen, April 2, 1948, even the pigmented remains of the greater part of the eruption had disappeared. These, however, were still present as brown patches on the fronts of the knees, on the palms, and on the left forefinger where the eruption recurs with her sore throats.

She has for long noticed that bruises appear on slight trauma of the skin, and formerly pressure and tension exerted on the skin of the palms, e.g. by wringing out clothes, produced linear hæmorrhagic streaks. These no longer occur.

Comments.—I have long held the view that Schamberg's dermatosis, in view of its histopathology, is probably caused by a hæmolytic toxin acting both on the blood cells and the walls of the capillaries. I have had many cases in which a chronic streptococcal infection, as in this case, proved to be responsible, and a few in which the eruption appeared suddenly after an acute infection, such as tonsillitis.

Dr. Barber then showed some coloured photographs of one of his early cases—an elderly man in whom the legs were extensively involved. He had been having injections of an autogenous hæmolytic streptococcal vaccine for a chronic throat infection. After his first visit he was evidently given an overdose of vaccine, which was followed by a rigor, high temperature, and the acute outbreak of his eruption on the back shown in the second photograph.

In another patient, seen during the past few years, the eruption, which became widespread, appeared when he was on active service after a septicæmic infection complicated by thrombophlebitis migrans. The point of interest in his case is that the organism responsible would seem to have been a strongly hæmolytic *Staphylococcus aureus*. He is now well.

The striking clinical resemblance of the eruption provoked in some persons by adalin to Schamberg's dermatosis would suggest that this drug may have an action on the red blood-corpuscles or capillaries comparable to that of certain bacterial toxins, but I have not seen microscopical sections of an adalin eruption. Dr. Yorke has recently had a patient who some years previously had had the characteristic adalin rash and in whom an acute outbreak of Schamberg's dermatosis had recently followed the extraction of infected teeth.

Parapsoriasis en Plaques Treated with Calciferol.—H. W. BARBER, F.R.C.P., and DAVID ERSKINE, M.D.

A. T. F., male. The eruption, which was extensive, involving the trunk and limbs, appeared gradually four or five years ago. There were no subjective symptoms. It improved under the influence of sunbathing in the summer. It was a characteristic example of parapsoriasis en plaques, of the type that resembles in its zoniform distribution pityriasis rosea. Some of the patches enclosed islets of normal skin, and the margins of others formed peninsulas and bays.

In the experience of one of us (H. W. B.) the only treatment that has had any lasting effect on this eruption has been exposure of the skin to sunlight or ultraviolet radiation. For this reason, one of us (D. E.) suggested that the patient should try the effect of calciferol. He had a course of twelve ampoules of sterogyl-15 (Roussel), and after a month's rest, a further course of six ampoules.

The effect has been remarkable, and when seen on March 31, 1948, the patches had faded leaving recognizable traces which appeared to show slight atrophy.

POSTSCRIPT.—On my advice, the patient took no more calciferol and the eruption gradually recurred.

I have had three other cases of parapsoriasis en plaques, all of which have responded to calciferol, but they will probably relapse when the treatment is discontinued.—H. W. B.

Parapsoriasis en Plaques—Treated with Vitamin D₂.—ALLAN YORKE, M.R.C.S., L.R.C.P. J. M., aged 28. Stoker.

Family history.—1940: Sister recovered from pulmonary tuberculosis.

History of present condition.—Eruption first appeared about June 1945 whilst he was serving in Italy, and involved parts covered by his trunks. Ardent sun-bather. It remained localized until return to this country in July 1946, when it spread centrifugally to abdomen, chest and then to the extremities, avoiding palms and soles. Moderate pruritus. Treated at several hospitals for "ringworm" with a variety of local applications.

On examination (September 1947).—Discrete, mobile, non-tender cervical glands of rubbery consistence. Multiple well-defined plaques or patches varying in colour from

red to fawn, and in size from a silver shilling to inches in diameter. The surfaces showed fine desquamation.

Blood-count within normal limits.

X-ray of chest: No evidence of organic disease.

Treatment (November and December 1947).—(1) Thorium X 1,000 units/c.c. was applied to the lesions of the upper arms on two occasions without significant change.

(2) As the initial lesions only involved the parts covered by the trunks, whilst sun-bathing freely in Italy, and as the lesions rapidly spread when these conditions were denied him on his return to this country, it was decided to give him vitamin D₂ 600,000 units orally at weekly intervals for four weeks.

The patient himself noticed regression at the end of two weeks, and when examined at the end of four weeks, (a) some lesions, i.e. the most recent, had disappeared completely. (b) Others showed significant regression, i.e. on the forearms. (c) The oldest lesions were involuting with hyperpigmentation.

The dark staining on the upper arms is an effect of thorium X.

Comment.—This patient was probably a tuberculous contact. His response to oral vitamin D₂ was rapid and definite. Even so, it may well be that parapsoriasis in this patient represents a tuberculide, which would accord with Civatte's opinion.

Multiple Atrophic Lesions: Case for Diagnosis.—C. D. EVANS, M.B.

Boy, aged 6 years.

History.—In January 1948 this boy had an attack of nocturnal delirium and pyrexia, lasting for a week. On the second day a bullous rash appeared. For the first two days he was given a medicine to reduce the temperature, but no other drugs were used except argyrol drops for a nasal discharge. When first seen on February 20 the condition was as follows:

On the arms and legs there were dark bluish plaques, 1 to 2 cm. in diameter, slightly raised above the surface and of irregular outline. On the trunk there were sharply defined bluish circular or oval lesions varying in size from $\frac{1}{2}$ to 3 cm. These were slightly depressed below the surface and showed some superficial atrophy and slight scaling. Many of the lesions had minute flesh-coloured papules scattered over their surface (fig. 1). Since

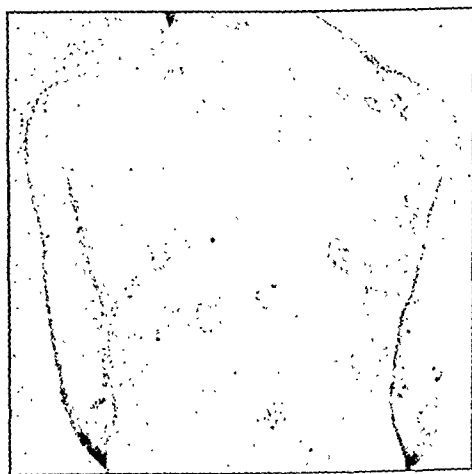


FIG. 1.—Photograph of lesions on the trunk.

February the lesions on the trunk have changed colour to a light red, those on the extremities remain dark blue but have tended to return to normal in the centre.

Past history.—Measles, whooping-cough and pneumonia at 2 years of age. A nasal discharge which started in infancy has persisted ever since in spite of treatment. He has had frequent chest trouble and has always been thin until recently.

In January 1947 he attended hospital and was diagnosed as suffering from a tuberculous hilar gland causing partial bronchial obstruction and collapse of the right middle and lower lobes, with bronchiectasis. He spent eight months in bed and then three months at a convalescent home.

Family history.—There is no history of tuberculosis. His mother died of "colitis".

Investigations.—Histology of lesion on back (Dr. Freudenthal): "The cutis shows a cellular scar tissue, probably rather a fresh scar, but there is no hint as to what the previous lesion may have looked like. The elastic fibres are thoroughly destroyed, with the exception of a few small spots where a number of thick fibres have survived. The epidermal changes, I suppose, are secondary".

Chest X-ray: The right hilar shadow is dense and enlarged, suggesting enlarged glands. There is partial deflation, with possible bronchiectatic changes in the right middle lobe and congestive or bronchiectatic changes in the posterior basal segment of the left lower lobe.

Blood-count.—R.B.C. 5.37 million; Hb 86%; C.I. 0.81; W.B.C. 9,600 (polys. 50%, eosinos. 2%, lymphos. 36%, monos. 12%).

Patch test with argyrol nasal drops was negative.

Mantoux test positive 1 : 10,000.

Note.—A further biopsy was done on a lesion from the left thigh on 22.4.48 when most of the induration had subsided. Section showed no microscopical evidence of tuberculous infection and the inflammatory reaction was minimal.

On 23.4.48 the child was admitted to hospital with a temperature of 101.5° F. A number of vesicles appeared in the lesions on the trunk which subsided in a day or so. The temperature returned to normal in three days and he returned home to rest in bed after fourteen days in hospital.

Dr. H. W. Barber: My opinion of this case is tentative as I could not examine the child as carefully as I should have wished. He reminded me of cases that were at one time not uncommon in which multiple patches of tuberculosis of the skin (disseminated lupus vulgaris) appeared after an acute infection, e.g. measles or whooping-cough. In such cases there is clearly bacillæmia, no doubt due, as Dr. Adamson suggested, to the breaking down of an old tuberculous focus with dissemination of the bacilli in the blood-stream. Dr. Cranston Lowe emphasized the fact that during and for some time after an attack of measles a von Pirquet reaction, which was previously positive, becomes negative, presumably due to antibodies disappearing from the skin. Hence, should a tuberculous bacillæmia occur, multiple patches of lupus are apt to appear instead of one or other of the tubercles in which the circulating bacilli are destroyed.

Fox-Fordyce Disease in a Young Girl.—R. T. BRAIN, M.D.

E. G., girl, aged 10.

History of a rash in the axillæ, on the breasts and on the pubic area of about twelve months' duration. The lesions irritate when she gets warm. Menstruation has not yet started but she has some secondary sexual changes indicating its imminence.

On examination.—She is a well-developed, intelligent girl, with pale pink papules in each axilla, a few pinkish papules on the areolæ of her breasts and a few papules on the mons veneris.

Since the clinical appearances are characteristic a biopsy has not been performed.

I have nothing to add to this case report except to point out the unusual feature of its early onset.

The President: Do you propose to use any hormonal treatment?

Dr. Brain: Not yet.

Necrobiosis Lipoidica Diabeticorum following Pyoderma.—F. RAY BETTLEY, F.R.C.P.

Mrs. H. H., aged 27.

History.—A known diabetic for seven to eight years. For the last four years recurrent sore throats.

October 1947: Attended the skin department of Middlesex Hospital with a slowly growing purple nodular area on the inner aspect of the left thigh, present for over six months. Thick yellowish pus exuded from a single small sinus.

Cultures: Coagulase positive *Staphylococcus pyogenes*.

Diagnosis: Chronic staphylococcal granuloma.

November 1947: Granuloma healed following local application of penicillin cream. Seen by Mr. Monkhouse, who advised tonsillectomy.

February 1948: Tonsillectomy. Urine showed sugar ++; acetone bodies ++.

Left thigh: Healed scar resulting from pyoderma now surrounded by an annular zone of typical necrobiosis lipoidica varying from 2 to 4 mm. wide.

March 6, 1948: Biopsy of left thigh showed typical necrobiosis.

March 7, 1948: Discharged from hospital. Diabetes balanced on diet and insulin.

April 1, 1948: Early patch of necrobiosis 1 cm. in diameter on left shin.

Comment.—I brought this patient because the occurrances in diameter. The surfaces showed injury has been mentioned many times and was recently I am not aware that it has been previously recorded as developing an infective lesion.

Sarcoidosis following Injury.—F. RAY BETTLEY, F.R.C.P.

Mrs. H. C., aged 37.

History.—1927: Road accident involving grazes and cuts of varying conditions were denied him 1943: Small sores began to appear in the scars. Seen in June 1943 by a D₂ 600,000 units orally when there were present irregular scars on the forehead with considerable and when examined at of dust in the scars. Scars excised July 1943. Healed satisfactorily. appeared completely. oldest lesions were

September 1947: Red nodules appeared on the scars, starting near the outer corner of the right eye.

November 1947: Similar nodule right pre-auricular. About the same time swelling of lymph glands in the neck was first noticed by the patient.

January 1948: Further yellow nodules appearing in the scar on the right side of the forehead. General health is fairly good. No loss of weight. No specific complaint.

On examination.—Irregular scarring, mainly linear, on the right side of the forehead around the orbit. Purplish and yellow-brown nodules are scattered in the scars. Large of these in the right upper eyelid measures 1½ cm. across while many are of pinhead size. In the right pre-auricular region is a similar nodule which has arisen without a preceding scar. There are many soft, not tender, lymph glands palpable on both sides of the neck.

Investigations.—X-ray: Chest—no hilar enlargement; lung fields normal; hands and feet normal.

Blood-count.—Hb 97%; W.B.C. 6,100. Differential normal.

Plasma proteins.—Albumin 4.2 grammes%; globulin 3.2 grammes%; fibrinogen 0.19 gramme %. Mantoux 1:1,000 positive. Blood Wassermann negative.

Histology.—Biopsy of nodule (right upper lid) shows well-formed typical sarcoidosis. (Section shown.)

Comment.—The original injuries resulted in scarring with a fair amount of tattooing of dust. Four years after these were excised nodules of sarcoid began to appear in the scars. After this there seems to have been a progress of the disease, starting in the scars and then appearing on the previously unaffected skin within the lymphatic drainage area, followed by involvement of the regional lymph glands. There are at present no other signs of sarcoidosis.

I would like to mention a similar occurrence in two previous cases. The first is a man whom I now have under treatment with sarcoidosis of the pernio type on the nose. In 1944 he had a car accident in which he grazed his nose against the windscreen. This resulted in a superficial injury which healed, leaving a small red scar. In May 1947 the scar started to become thickened, and ultimately changed into a typical sarcoid covering an area two or three inches across. The diagnosis was confirmed by biopsy and there are no other lesions.

The third case of this kind is a medical student who had superficial scars on the tip of the nose resulting from a slight injury. When I saw him in April 1946 the scars were becoming red and nodular and a small nodule had appeared on the upper lip. Biopsy showed typical sarcoidosis. Dr. Leonard Howells saw this patient, and found radiological evidence of enlarged hilar glands with a fine nodulation in the lung parenchyma compatible with sarcoidosis. The Mantoux test 1/1,000 was positive; blood-count, E.S.R., skiagram of the feet, were all normal. I have not seen him since, but Dr. Leonard Howells kindly informs me that the skin lesions have not appeared; the radiological appearances in the chest are unchanged but no other sarcoidosis has appeared.

These cases are of importance because the cause of sarcoidosis remains unknown. It is usually assumed that the disease has been able to discover any information or evidence as to its origin.

Those who have assumed the disease is developing at remote sites. These followed, in the time of injury. Other possible

Family history.—There is no history as determined the onset of sarcoidosis in these particular sites.

Investigations.—Histology of cellular scar tissue, probably of a few small spots where lesion may have looked like Bloch and Sulzberger).—HENRY HABER, M.D.

I suppose, are secondarily a rash on right arm, which became generalized on the fourth day.

Chest X-ray: The r. Eruption on the trunk consisting of tense vesicles arranged in some There is partial degeneration forming a reticular pattern. Warty lesions on the proximal segments of congestive or bronchial. Blue scleræ. Twitches occasionally. Otherwise nil.

Blood-count.—Eosinophils. 2%. Lymphocytes. Blood-count normal.

Patch test was given sulphapyridine tablets for pneumonia when seven months pregnant.

Mantoux negative. No similar skin trouble in the family. The rash has undergone changes during the last ten months.

Note.—The changes during the last ten months.

Examination.—The vesicular eruption has disappeared entirely. It has been replaced by a peculiar pigmented rash of a characteristic grey-brown colour, shape, and arrangement.

On individual lesion is an atrophic macule or a bizarre line which does not follow any reticuli or nerves, the whole pattern suggests something artificial or arbitrary, never seen in history, and is characteristic for the dermatosis.

The warty lesions have undergone considerable involution and there are only a few lesions on the left thigh present.

Incontinentia pigmenti is a well-defined histological dermatological entity described by Bloch and Sulzberger. It is characterized by the following features:

- (1) Presence of lesions at birth or first days of life.
- (2) Obscure inflammatory condition of skin, such as bullous erythema, urticaria, precedes pigmentation.
- (3) Associated with the pigmentary anomaly there are sometimes other ectodermal defects.
- (4) Dermatoses may show a familial occurrence.
- (5) It has a characteristic histology. There is only slight epidermal change confined to the basal-cell layer, which shows various degrees of irregularity and hydrops of individual cells, and some smaller cells with pyknotic nuclei. In general, the pigment in the epidermis is not increased, and only slightly increased in certain areas. The stratum papillare and subpapillare show the presence of coarse melanin granules, situated within phagocytic cells. Bloch and Sulzberger forwarded a hypothesis that there is a congenital pigmentary anomaly due to a pathological permeability of the melanoblasts by which the pigment instead of being discharged into the epidermis is directed into the corium, leading to an autochthonous tattoo of the corium. This tattoo is responsible for the peculiar pattern.
- (6) The pigmentation is of such striking appearance that once seen it can never be missed again.

Dr. W. N. Goldsmith: Is the pigmentation always preceded by the various inflammatory conditions described? If so, the name is very inadequate for the clinical disorder as a whole. It only expresses a histologically diagnosed pigmentary aberration. Do the patches all look brown rather than grey or blue, in spite of the masses of pigmentation being fairly deep in the dermis, the epidermis being practically empty of it?

Dr. Haber: Bloch and Sulzberger labelled their case *Incontinentia Pigmenti* because they thought that the melanoblasts of the basal layer are unable to keep their pigment within the cell membrane. Siemens, who was not prepared to accept the Bloch-Sulzberger theory, labelled his case as a "melanotic degeneration of the corium" and Naegeli regarded the condition as a chromatophore nevus. The colour of the pigmentation is similar to that of arsenical and tar melanosis because the chromatophores are situated in the upper layers of the corium, whereas in the blue nevus the melanoblasts are to be found in the mid-cutis.

The following cases were also shown:

Case for Diagnosis. ? Leiomyoma.—Dr. G. B. DOWLING.

Riehl's Melanosis (Type Civatte).—Dr. E. J. MOYNAHAN (for Dr. L. FORMAN).

Pityriasis Rubra Pilaris.—Dr. D. I. WILLIAMS.

(1) *Erythema Figuratum Perstans*. (2) *Atrophoderma Vermiculata*.—Dr. THERESA KINDLER.

(These cases may be published later in the *British Journal of Dermatology*.)

Comment.—I brought this patient because the occurrence of injury has been mentioned many times and was recently. I am not aware that it has been previously recorded as developing an infective lesion.

Sarcoidosis following Injury.—F. RAY BETTLEY, F.R.C.P.

Mrs. H. C., aged 37.

History.—1927: Road accident involving grazes and cuts of varying dimensions on the trunks, whilst sun-bathing. Conditions were denied him. 1943: Small sores began to appear in the scars. Seen in June 1943 by Dr. D. 600,000 units orally when there were present irregular scars on the forehead with considerable dust in the scars. Scars excised July 1943. Healed satisfactorily. September 1947: Red nodules appeared on the scars, starting near the outer corner of the right eye. When examined at the oldest lesions were

November 1947: Similar nodule right pre-auricular. About the same time swelling of lymph glands in the neck was first noticed by the patient.

January 1948: Further yellow nodules appearing in the scar on the right side of the forehead. General health is fairly good. No loss of weight. No specific complaint.

On examination.—Irregular scarring, mainly linear, on the right side of the forehead around the orbit. Purplish and yellow-brown nodules are scattered in the scars. Large of these in the right upper eyelid measures $1\frac{1}{2}$ cm. across while many are of pinhead size. In the right pre-auricular region is a similar nodule which has arisen without a preceding scar. There are many soft, not tender, lymph glands palpable on both sides of the neck.

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Histology.—Biopsy of nodule (right upper lid) shows well-formed typical sarcoidosis. (Section shown.)

Comment.—The original injuries resulted in scarring with a fair amount of tattooing of dust. Four years after these were excised nodules of sarcoid began to appear in the scars. After this there seems to have been a progress of the disease, starting in the scars and then appearing on the previously unaffected skin within the lymphatic drainage area, followed by involvement of the regional lymph glands. There are at present no other signs of sarcoidosis.

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The third case of this kind is a medical student who had superficial scars on the tip of the nose resulting from a slight injury. When I saw him in April 1946 the scars were becoming red and nodular and a small nodule had appeared on the upper lip. Biopsy showed typical sarcoidosis. Dr. Leonard Howells saw this patient, and found radiological evidence of enlarged hilar glands with a fine nodulation in the lung parenchyma compatible with sarcoidosis. The Mantoux test 1/1,000 was positive; blood-count, E.S.R., skiagram of the feet, were all normal. I have not seen this patient since, but Dr. Leonard Howells kindly informs me that the skin lesions have now disappeared; the radiological appearances in the chest are unchanged but no other sign of sarcoidosis has appeared.

These cases are of importance so long as the cause of sarcoidosis remains unknown. It is usually assumed to be an infection, but I have not been able to discover any information or evidence as to the portal of entry.

Those who lean to the view that sarcoidosis is tuberculous in origin will presumably assume the usual portals of entry for that disease, with sarcoidosis developing at remote sites. These three cases, however, suggest the inoculation of infection at the time of injury followed, in the first patient, by a progressive spread via the lymph channels. Other possible

tissue in the corium. There is no obvious decrease in the amount of elastic tissue present.

The interest of this case lies in the fact that up till three months ago when his son developed the condition he would by many have been labelled as a case of epidermolysis bullosa acquisita, a not very happy name.

II.—B. E., male, aged 4 months. Only child.

History.—At the aged of 1 month the mother noticed that blisters were developing on the hands and fingers after the baby had sucked them. Later it was realized that slight knocks also produced blisters. "White little lumps" were first noticed on the backs of the hands at the age of 6 weeks.

The baby is otherwise thriving.

Family history.—Apart from the father no other relatives are known to be affected. The parents are not related.

On examination.—Clusters of milium-like bodies are present on the backs of the hands, identical with those on the father's hands. The remains of blebs are seen and on two occasions unbroken blebs containing clear fluid were observed on the fingers and on the palm of one hand.

Tropical Lichenoid Dermatitis.—K. GREENWOOD, M.B., M.R.C.P., Major R.A.M.C.

The eruptions due to idiosyncrasy to mepacrine have been described by, among others, Nisbet (1945) Schmitt, Alpins and Chambers (1945), and Singh (1948).

Nisbet described the condition as accounting for 80% of total dermatological cases received at his hospital from New Guinea. He says that certain characteristics help in its identification. A tendency to pigmented, flat, or hypertrophic lichenoid lesions, the production of persistent circumscribed erythematous areas, the characteristic distribution, extreme chronicity, a decided tendency to secondary infection, a tendency to progress to an exudative eczematous eruption, and peculiar pigmentary changes.

He describes three types: The patchy eczematoid type, the hypertrophic lichenoid type, and a generalized exfoliative type.

This second type, as in the present case, is very similar to hypertrophic lichen planus. Lesions on the eyelids are particularly common. The patients may be profoundly ill.

The blood picture is essentially normal, but shows sometimes a leucocytosis and an eosinophilia.

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- NISBET, T. W. (1945) A New Cutaneous Syndrome Occurring in New Guinea and Adjacent Islands, *Arch. Derm. Syph., Chicago*, 52, 221.
 SCHMITT, C. L., ALPINS, O., and CHAMBERS, G. (1945) Clinical Investigation of a New Cutaneous Entity, *Arch. Derm. Syph., Chicago*, 52, 286.
 SINGH, I. (1948) *Brit. J. Derm.*, 60, 90.
 Dr. R. C. E. Brodie (Melbourne): I have seen about 400 of these cases. The variety shown this afternoon is the true hypertrophic type. One case which I saw recently had persisted for four years. I myself have now seen it for three years and there have been no signs of regression. The case is symptomless, but there is often intense pyrexia on exertion on a warm day. I was interested in seeing the case now shown because it corresponds to the general experience. I am sorry I cannot help in the matter of treatment.

Dr. H. Haber: I have seen a case with moth-eaten alopecia, which at first I thought to be due to syphilis.

The following cases were also shown:

Case for Diagnosis. ? Necrobiosis Lipoidica.—Dr. LOUIS FORMAN.

Recurrent Ulcers of the Mouth with a Family History of a Similar Condition.—Dr. LOUIS FORMAN and Mr. G. B. PRITCHARD.

(1) Bullous Eruption, ? Due to a Virus. (2) Bowen's Disease.—Dr. C. H. WHITTLE and Dr. A. LYELL.

Case for Diagnosis. ? Tuberculide.—Dr. J. MARTIN BEARE for Dr. H. J. WALLACE.

Dermatomyositis, Scleroderma, Calcinosis Universalis, High Serum Calcium.—Dr. J. R. OWEN and Dr. BASIL STRICKLAND.

Lupus Erythematosus with Unusual Features.—Dr. D. S. WILKINSON for Dr. G. C. WELLS.

Pemphigus Foliaceus.—Dr. E. J. MOYNAHAN.

Rosacea-like Tuberculide.—Dr. PATRICK HALL-SMITH (introduced by Dr. W. J. O'DONOVAN).

Mikulicz' Disease.—Dr. G. B. MITCHELL-HEGGS and Dr. M. FEIWEL.

(1) Hemochromatosis (Without Glycosuria). (2) Tylosis Palmæ et Plantæ. (3) Urticaria Pigmentosa.—Dr. I. R. MARRE.

(These cases may be published later in the *British Journal of Dermatology*.)

[May 20, 1948]

Precocity in a Girl Aged 5 : Due to Stilbæstrol Inunction.—C. H. WHITTLE, M.D., and A. LYELL, M.B.

Patient S. H. This child had total alopecia from 1 year of age after chickenpox and otitis media.

In December 1947 she was given stilbæstrol ointment 0.5% to rub into the scalp, and the mother continued to use this for thirteen weeks. After about ten weeks' treatment vaginal bleeding was noticed and was fairly heavy for a week, and continued for about four weeks, for the last week of which she was under observation in hospital.

For the last two or three months there has been deep pigmentation of the areolæ of the breasts, and the breasts have developed and become prominent. There is deep pigmentation also of the trunk.

Investigation in hospital showed a healthy well-grown child, with rather a deep voice. The scalp hair appears to be growing: eyebrows present, eyelashes present but scanty on lower lids. No pubic or axillary hair.

Dosage: 2 ounces of ointment (emulsifying base) yield 240 mg. of stilbæstrol, or approximately 2.7 mg. daily if *all* were absorbed.

Special examinations.—(1) 17-ketosteroid output 1.7 mg. *per diem*, i.e. normal. (2) X-ray of the skull—sella turcica normal.

Comment.—Dr. Laurence Martin saw the child and stated that he thought this was a pure stilbæstrol effect. He suggested as an alternative diagnosis a true constitutional precocious puberty. If the first alternative is rejected, the second may be the correct one, the stilbæstrol either drawing attention to or accentuating the condition. But the bleeding has ceased and the breasts are getting smaller since the stilbæstrol was stopped.

POSTSCRIPT (3.7.48).—Dr. H. W. Barber writes (personal communication): "As compared with the effects of oral administration of tablets in usual dosage, there is no doubt that inunctions are far more active, and must be used with the greatest care. The explanation, no doubt, is that some of the œstrogen, when rubbed into the skin, is absorbed into the blood-stream and exerts its effects before being altered by the liver, whereas when given by mouth all of it, of course, has to pass through the liver before reaching the blood-stream. I have had many cases in which uterine bleeding and pigmentation of the nipples have followed in a short time the inunction of dienœstrol ointment into the scalp or face of women long past the menopause, and it is extremely rare for pigmentation of the nipples to result even from high doses of œstrogen *by mouth* after the menopause, the excess of pituitary gonadotrophins being supposed in some way to check pigmentation. Stilbæstrol is many times more potent than dienœstrol, so I am not surprised at the effects in this case."—C. H. W.

Epidermolysis Bullosa, Two Cases (Father and Son).—DAVID I. WILLIAMS, M.R.C.P.

I.—J. E., male, aged 22.

History.—In 1943 when he was a stoker in the Royal Navy he began for the first time in his life to develop an eruption involving the hands, the feet and the knees. He was seen by several dermatologists, who diagnosed chronic dermatitis and prescribed various ointments with no avail. In August 1946 X-rays, 200 r, were applied to the hands and repeated in three weeks.

On 16.11.46 the following report was made: "Teeth adequate: the skin of both elbows and knees shows hyperkeratosis and pigmentation. Both legs from knees to ankles show marked pigmentation with several small ulcers covered by scabs. Diagnosis: 'Dermatitis'."

A further report on 20.10.47 states: "There are patches of dermatitis on ankles, knees, back of hands, across the shoulders and on the front of the chest. Lesions consist of small milky-white papules which break down and form superficial ulcers; a few blood cysts are present on the hands. There is progressive loss of the toe-nails and a similar condition is beginning on the hands."

He receives a 25% disability pension.

Past history.—Uneventful.

Family history.—Until his son, now aged 4 months, developed the condition at the age of 1 month, no member of his family was known to suffer from a similar complaint.

On examination.—He shows the typical scars of the condition on the knees, hands and feet. Bullæ containing clear fluid have been seen from time to time. He has lost his toe-nails and is losing the finger-nails. He has multiple milium-like bodies on the backs of the hands.

Histological report (Prof. H. A. Magnus).—Section shows the typical histological picture of epidermolysis bullosa dystrophica with some increase in the amount of fibrous

Biopsy (Dr. A. M. Barrett).—Section taken from these circular and oval pale scars shows gross abnormality of the superficial layer of the corium. The delicate inter-papillary zone with its tree-like branching elastic fibres is almost absent and instead there is a dense feltwork of elastic fibres slightly below the bases of the poorly developed papillae with only a few twigs sprouting up towards the epidermis. The interpapillary layer is thus thinner, denser and less rich in elastic tissue than normal.

Blood: Wassermann and Kahn reactions are negative.

Dr. Whittle: This is obviously a case of epidermolysis bullosa of the dystrophic type, but we have been specially interested in the white circular areas on the lower part of the trunk. All the activity appears to have been on the shoulders and the legs. We therefore tried to find out whether the atrophic lesions were really part of the disease picture. Sections showed considerable thinning of the skin, chiefly in the papillary layer. The normal elastic layer is completely absent and instead, in the thinned corium, there is a coarse feltwork of broken-up elastic tissue.

Cockayne (1933) mentions a *typus maculatus* which occurred in non-familial cases in Holland: there were two sisters similarly affected. Cerutti (1933) also described two cases of epidermolysis bullosa with an "albo-papuloid dystrophy"—white wrinkled areas of 2 cm. diameter scattered all over the trunk and surrounded by hyperpigmentation. We would welcome suggestions as to the cause of these lesions, and whether their pathology is linked with that of epidermolysis bullosa.

REFERENCES

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 COCKAYNE, E. A. (1933) *Inherited Abnormalities of the Skin*. London, p. 132.

Dr. G. B. Dowling: I would like to refer Dr. Whittle to the report of an identical case (Degos, R. et al. (1948) *Bull. Soc. Dermat. Syph.*, p. 164) under the name of Epidermolyse bulleuse congénitale dystrophique, type albo-papuloides de Pasini.

Dr. R. T. Brain: I have seen several cases of the atrophic type of epidermolysis bullosa; with them we have seen the nails atrophy without receiving bullosus damage to the matrix.

Dr. Dowling: The principal feature of this condition is the presence of firm white papules seen mainly on the trunk and not preceded by bullae.

Hyperkeratosis Follicularis et Para-follicularis in Cutem Penetrans (Kyrle).—RONALD SCUTT, M.B. (for R. M. B. MACKENNA, M.D.).

Mrs. M. C., aged 60.—Non-irritating spots on the legs for two years, slowly increasing in size. No history of relevant illnesses nor of intake of drugs.

Scattered over lower legs are numerous reddish-brown papules varying in size from pinhead to split pea. Smaller lesions show central horny plugs, leaving small craters on removal. Larger lesions show irregular greyish-yellow horny crusts, with an inflammatory halo of the surrounding skin. Some of the older lesions have healed, leaving small depressed scars. No lesions elsewhere.

Investigations.—W.R., Kahn, negative. Blood-count: Mild normocytic anaemia, otherwise within normal limits. Vitamin-A value—Carotenoids 233 i.u./100 ml., vitamin A 79 i.u./100 ml.

Histology report (Dr. H. Haber).—"The section shows two lesions, both of which represent a parakeratotic plug pressing heavily on the underlying epidermis, which forms broad shallow grooves on which the horny masses rest. In no place is there any tendency for these plugs to penetrate the cutis, which shows a mild inflammatory reaction."

Comments.—This case, only the second to be published in this country, shows the clinical characteristics as originally described by Kyrle (*Arch. Derm. Syph. Chicago*, 1916, 123, 466). Until 1947, when Arnold reviewed the literature, only about 12 cases had been written up, practically all in the German and Danish journals, though Benedek and Oreo then stated that they had seen several cases, all in negro soldiers. When Dr. J. R. Simpson showed his case in December 1946 (*Proceedings R. Soc. Med.*, 40, 262), Dr. Hohmann said that he had seen cases in Holland in which the serum vitamin-A values had been low, and in which improvement had occurred after prolonged administration of the vitamin. In this case, the vitamin-A values are within normal limits.

The non-penetration of the cutis indicates either that the excised lesion is an early one, or that Kyrle's conception of the pathology was not entirely accurate. Also, there appears to be no definite relationship to hair follicles. Arnold described a case in which lesions were present in the palms only, where, of course, there are no hair follicles. These minor differences are possibly sufficient, as Arnold pointed out, to reduce the unwieldy name of this disease to "hyperkeratosis penetrans".

[June 17, 1947]

Pretibial Myxomatous Degeneration.—C. D. CALNAN, M.B. (for I. MUENDE, M.R.C.P.).

Miss L. W., aged 47.

History.—1941: Partial thyroidectomy for Graves' disease.

1943: Kicked on right shin.

1944: In the course of a few days the skin on the front of the legs became tense and swollen as it appears at present.

1947: Normal menopause.

February 1948: Began to complain of giddiness and palpitation, feeling hot and cold, and was referred by her doctor who found her in an emotional state with a tachycardia of 120/min.

On examination.—Somewhat obese. Outer third of eyebrows thin. Some fullness under the eyes. No exophthalmos. Heart, lungs, abdomen normal. Pulse-rate 60/min. Blood-pressure 160/80.

An "œdema-like" swelling is present on the anterior aspect of both legs between the knees and ankles, spreading on to the posterolateral surface in its lower part. The area is pale reddish-brown with prominent follicles and a few coarse hairs. The upper limit shows a gradual transition from normal skin to the swollen area. The lower margin, however, is sharply demarcated, and shows the maximum swelling of 4 to 5 mm. The area is firm and does not pit on pressure. At the side the transition to normal skin is irregular and there are many small round lesions of similar tissue. A rather more elevated area in the centre of the lesion in the right leg is at the site of injury in 1943.

Investigations.—Blood cholesterol 138 mg./100 ml. E.C.G.: Normal; no evidence of myxœdema. B.M.R. -9%.

Biopsy (Dr. H. C. Moore).—Section shows myxomatous degeneration of subepidermal tissues which occurs in masses with no intervening collagen, and stains with Southgate's mucicarmine. Mallory's stain is not taken up by the myxomatous areas.

Treatment—1944: Extr. thyroid sicc., gr. $\frac{1}{2}$ b.d. for one year.

1945: Extr. thyroid sicc., gr. $\frac{1}{2}$ t.d.s., up to present time.

No striking improvement has been noted in the condition, in spite of four years' treatment with thyroid extract.

Comment.—This is a case of extensive localized pretibial myxomatous degeneration, occurring three years after partial thyroidectomy for thyrotoxicosis.

Dr. F. Parkes Weber: This is one of those cases which should appear in an international atlas of dermatology. It is so striking and yet so typical in every way. The mucinous plaques over the shins are of extreme degree. The patient has had thyrotoxicosis and has been operated for it. A permanent record is needed for teaching purposes.

Dr. Lipman Cohen: The one atypical feature in this patient is the degree of pinkness of the lesion which is usually much more yellow, rather like pigskin.

Epidermolysis Bullosa Dystrophica (with "Albo-papuloid Dystrophy" of Pasini).—C. H. WHITTLE, M.D., and A. LYELL, M.B.

F. R. a farm labourer, aged 43.

History of sores on the back and the legs which are said to have started after vaccination at the age of 6 months. They have been present on and off ever since.

Family history (not completed).—Two sisters have similar sores though less severe.

When he was first seen nine years ago the lesions were typical on the legs and on the shoulders, with large blisters leaving sores which healed slowly. Two years ago he had superimposed sepsis which masked the picture so much that the diagnosis of epidermolysis bullosa was not considered until his original notes were turned up. There was severe chronic ulceration on the left leg and the shoulder. Hæmolytic strep. and *Staph. aureus* were obtained in abundance in cultures.

The condition has waxed and waned so that at times he has been almost completely free of blisters; in addition there are curious scars on the trunk quite different from those on the shoulders and legs. These are circular and oval, white, crinkled, rather papery areas varying from 1 to 4 cm. in diameter, of uniform consistency and occurring in large numbers. They have been present for as long as he can remember and he is positive that they are not the result of blisters. In these white areas the skin is thinner and feels soft.

Biopsy (Dr. A. M. Barrett).—Section taken from these circular and oval pale scars shows gross abnormality of the superficial layer of the corium. The delicate inter-papillary zone with its tree-like branching elastic fibres is almost absent and instead there is a dense feltwork of elastic fibres slightly below the bases of the poorly developed papillae with only a few twigs sprouting up towards the epidermis. The interpapillary layer is thus thinner, denser and less rich in elastic tissue than normal.

Blood: Wassermann and Kahn reactions are negative.

Dr. Whittle: This is obviously a case of epidermolysis bullosa of the dystrophic type, but we have been specially interested in the white circular areas on the lower part of the trunk. All the activity appears to have been on the shoulders and the legs. We therefore tried to find out whether the atrophic lesions were really part of the disease picture. Sections showed considerable thinning of the skin, chiefly in the papillary layer. The normal elastic layer is completely absent and instead, in the thinned corium, there is a coarse feltwork of broken-up elastic tissue.

Cockayne (1933) mentions a *typus maculatus* which occurred in non-familial cases in Holland: there were two sisters similarly affected. Cerutti (1933) also described two cases of epidermolysis bullosa with an "albo-papuloid dystrophy"—white wrinkled areas of 2 cm. diameter scattered all over the trunk and surrounded by hyperpigmentation. We would welcome suggestions as to the cause of these lesions, and whether their pathology is linked with that of epidermolysis bullosa.

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Dr. G. B. Dowling: I would like to refer Dr. Whittle to the report of an identical case (Degos, R. et al. (1948) *Bull. Soc. Dermat. Syph.*, p. 164) under the name of Epidermolysse bulleuse congénitale dystrophique, type albo-papuloides de Pasini.

Dr. R. T. Brain: I have seen several cases of the atrophic type of epidermolysis bullosa; with them we have seen the nails atrophy without receiving bullous damage to the matrix.

Dr. Dowling: The principal feature of this condition is the presence of firm white papules seen mainly on the trunk and not preceded by bullae.

Hyperkeratosis Follicularis et Para-follicularis in Cutem Penetrans (Kyrle).—RONALD SCUTT, M.B. (for R. M. B. MACKENNA, M.D.).

Mrs. M. C., aged 60.—Non-irritating spots on the legs for two years, slowly increasing in size. No history of relevant illnesses nor of intake of drugs.

Scattered over lower legs are numerous reddish-brown papules varying in size from pinhead to split pea. Smaller lesions show central horny plugs, leaving small craters on removal. Larger lesions show irregular greyish-yellow horny crusts, with an inflammatory halo of the surrounding skin. Some of the older lesions have healed, leaving small depressed scars. No lesions elsewhere.

Investigations.—W.R., Kahn, negative. Blood-count: Mild normocytic anaemia, otherwise within normal limits. Vitamin-A value—Carotenoids 233 i.u./100 ml., vitamin A 79 i.u./100 ml.

Histology report (Dr. H. Haber).—"The section shows two lesions, both of which represent a parakeratotic plug pressing heavily on the underlying epidermis, which forms broad shallow grooves on which the horny masses rest. In no place is there any tendency for these plugs to penetrate the cutis, which shows a mild inflammatory reaction."

Comments.—This case, only the second to be published in this country, shows the clinical characteristics as originally described by Kyrle (*Arch. Derm. Syph. Chicago*, 1916, 123, 466). Until 1947, when Arnold reviewed the literature, only about 12 cases had been written up, practically all in the German and Danish journals, though Benedek and Oreo then stated that they had seen several cases, all in negro soldiers. When Dr. J. R. Simpson showed his case in December 1946 (*Proceedings R. Soc. Med.*, 40, 262), Dr. Hohmann said that he had seen cases in Holland in which the serum vitamin-A values had been low, and in which improvement had occurred after prolonged administration of the vitamin. In this case, the vitamin-A values are within normal limits.

The non-penetration of the cutis indicates either that the excised lesion is an early one, or that Kyrle's conception of the pathology was not entirely accurate. Also, there appears to be no definite relationship to hair follicles. Arnold described a case in which lesions were present in the palms only, where, of course, there are no hair follicles. These minor differences are possibly sufficient, as Arnold pointed out, to reduce the unwieldy name of this disease to "hyperkeratosis penetrans".

[June 17, 1947]

Pretibial Myxomatous Degeneration.—C. D. CALNAN, M.B. (for I. MUENDE, M.R.C.P.). Miss L. W., aged 47.

History.—1941: Partial thyroidectomy for Graves' disease.

1943: Kicked on right shin.

1944: In the course of a few days the skin on the front of the legs became tense and swollen as it appears at present.

1947: Normal menopause.

February 1948: Began to complain of giddiness and palpitation, feeling hot and cold, and was referred by her doctor who found her in an emotional state with a tachycardia of 120/min.

On examination.—Somewhat obese. Outer third of eyebrows thin. Some fullness under the eyes. No exophthalmos. Heart, lungs, abdomen normal. Pulse-rate 60/min. Blood-pressure 160/80.

An "œdema-like" swelling is present on the anterior aspect of both legs between the knees and ankles, spreading on to the posterolateral surface in its lower part. The area is pale reddish-brown with prominent follicles and a few coarse hairs. The upper limit shows a gradual transition from normal skin to the swollen area. The lower margin, however, is sharply demarcated, and shows the maximum swelling of 4 to 5 mm. The area is firm and does not pit on pressure. At the side the transition to normal skin is irregular and there are many small round lesions of similar tissue. A rather more elevated area in the centre of the lesion in the right leg is at the site of injury in 1943.

Investigations.—Blood cholesterol 138 mg./100 ml. E.C.G.: Normal; no evidence of myxœdema. B.M.R. -9%.

Biopsy (Dr. H. C. Moore).—Section shows myxomatous degeneration of subepidermal tissues which occurs in masses with no intervening collagen, and stains with Southgate's mucicarmine. Mallory's stain is not taken up by the myxomatous areas.

Treatment—1944: Extr. thyroid sicc., gr. $\frac{1}{4}$ b.d. for one year.

1945: Extr. thyroid sicc., gr. $\frac{1}{4}$ t.d.s., up to present time.

No striking improvement has been noted in the condition, in spite of four years' treatment with thyroid extract.

Comment.—This is a case of extensive localized pretibial myxomatous degeneration, occurring three years after partial thyroidectomy for thyrotoxicosis.

Dr. F. Parkes Weber: This is one of those cases which should appear in an international atlas of dermatology. It is so striking and yet so typical in every way. The mucinous plaques over the shins are of extreme degree. The patient has had thyrotoxicosis and has been operated for it. A permanent record is needed for teaching purposes.

Dr. Lipman Cohen: The one atypical feature in this patient is the degree of pinkness of the lesion which is usually much more yellow, rather like pigskin.

Epidermolysis Bullosa Dystrophica (with "Albo-papuloid Dystrophy" of Pasini).—C. H. WHITTLE, M.D., and A. LYELL, M.B.

F. R. a farm labourer, aged 43.

History of sores on the back and the legs which are said to have started after vaccination at the age of 6 months. They have been present on and off ever since.

Family history (not completed).—Two sisters have similar sores though less severe.

When he was first seen nine years ago the lesions were typical on the legs and on the shoulders, with large blisters leaving sores which healed slowly. Two years ago he had superimposed sepsis which masked the picture so much that the diagnosis of epidermolysis bullosa was not considered until his original notes were turned up. There was severe chronic ulceration on the left leg and the shoulder. *Hæmolytic strep.* and *Staph. aureus* were obtained in abundance in cultures.

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Section of Psychiatry

President—Professor Sir DAVID K. HENDERSON, M.D., F.R.C.P., F.R.S.E.

[May 18, 1948]

The Management and Treatment of Psychopaths in a Special Institution in Denmark

By GEORG K. STÜRUP, M.D.

IN order to understand the unusual working conditions which have gradually been introduced in the Herstedvester Institution for Psychopaths it is necessary to explain briefly the special legislation which provides the framework for the treatment of psychically abnormal criminals and borderline cases.

The Herstedvester Institution has two main purposes: To protect society and maintain public security by means of the preventive detention of the inmates of the Institution, and secondly, to treat these inmates psychologically in order to fit them for a normal life as free citizens.

In a number of cases, therefore, detention may be of short duration. It is not a punishment, but a security measure. By far the majority of the detainees are relapsed criminals who have committed serious crimes—murder, robbery, incendiarism, rape, indecency towards boys or girls or both, theft, embezzlement, crimes of violence—but we have also drug

TABLE I.—DOMINANT CRIMINALITY OF THE 300 FIRST DETAINEES IN HERSTEDVESTER

Theft	94
Fraud	22
Breaking confidence	31
Sexual crimes against children	88
Exhibitionism	15
Rape	10
Arson	16
Violence (incl. homicide)	13
Polycriminality	11
Total	300

TABLE II.—DIAGNOSES FOR THE 300 FIRST DETAINEES IN HERSTEDVESTER

		%
Character insufficiency ..	218	73
Character abnormality ..	9	3
Imbecility	1	0
Intellectual inferiority ..	72	24
Psycho-infantility	54	18
Neurosis	69	23
Psychosis	24	8
Epilepsy	23	8
Organic diseases in C.N.S.	16	5
Alcoholism	36	12

addicts who forge prescriptions and similar cases where other forms of treatment have proved ineffective (Tables I and II). Most of them have been in prison again and again. Only a few outstandingly psychiatric cases reach the Institution for Psychopaths after the first or second court sentence. The detainees vary in age from about 18 to 70 years.

In sentencing persons to detention in the Institution the courts do not prescribe any definite period and the same court which has passed sentence decides whether the detainee may be released. Release is always subject to parole the period of which is likewise not defined. During parole the prisoner is subjected to supervision directly from the institution. This supervision is carried out by officers specially trained by the institution, and the paroled person may not change his place of residence or employment without obtaining the prior approval of the institution. Final release is likewise only obtainable on application to the same court which ordered detention and parole.

There must therefore be an intimate co-operation between the court and the psychiatrist responsible for the treatment which is given during detention. The first Act dealing with this question came into force in 1925. This Act provided for the internment of certain abnormal criminals who constitute a palpably serious danger to the public safety, defined in the Act as including sexual offences, gross acts of violence, incendiarism or other serious crimes. A new criminal law of 1930 which, since 1933, is still in force to-day affords a sub-

Dr. Haber: Kyrle's first case of *Hyperkeratosis follicularis et parafoollicularis in cutem penetrans* was a woman, aged 22, who developed a generalized rash in the course of a few weeks. The primary lesion consisted of a pinhead hyperkeratosis, partly follicular and partly parafoollicular. As the lesion grew it became indurated, and there was an inflammatory halo round it. The lesions tended to coalesce to larger plaques and the colour became dirty green-brown similar to that seen in psoriatic rupia. On removal of a plaque bleeding occurred and a depressed scar was left after healing. The head, hands and feet were free from lesions. Kyrle performed many biopsies on the case and found follicular and parafoollicular hyperkeratotic plaques extending deep to the pallisade layer and sometimes perforating the latter, producing a foreign-body reaction. He regarded the condition as a dyskeratosis.

Many more cases were described after Kyrle's paper, but some authors stressed the point that penetration does not always take place. In this case one can see that the hyperkeratosis is pressing on the epidermis causing thinning of the latter, but actual penetration does not take place. Another section showed almost penetration with an inflammatory reaction in the cutis, so that penetration is not obligatory and the downgrowth of the hyperkeratosis only a matter of degree.

The clinical picture combined with the histological findings justify the title given to the disease.

Dr. W. Lemberger: Further biopsies should be done to demonstrate other peculiar features of this condition in an earlier stage. The prickle cells are in some places strikingly small and packed so closely together that the intercellular spaces almost disappear. There are also marked degenerative changes in the cytoplasm and the cell nuclei.

Dr. John C. Belisario (Sydney): In a case presented in America with the same diagnosis only the palms and soles were affected. The opinion was that the condition was allied with keratosis punctata or lichen pilaris, which in turn is considered by many to be linked with ulerythema ophryogenes and keratosis follicularis ulerythematosus.

Dr. John C. Belisario (Sydney) read a paper on *Cutaneous Cancer and Precancer* (to appear later in the *British Journal of Dermatology*).

The following cases were also shown:

Case for Diagnosis.—**Dr. C. H. WHITTLE.**

Nævus Syringadenomatosus Papilliferus.—**Dr. JAMES OVERTON.**

Papulonecrotic Tuberculide with Acne Scrofulosorum.—**Dr. J. R. SIMPSON.**

Reticulosis.—**Dr. W. G. TILLMAN.**

(These cases may be published later in the *British Journal of Dermatology*.)

follows a period of bitter disappointment, the indeterminate sentence begins to get on his nerves and very often there ensues a feeling of hopelessness. At this juncture the detainee, under suitable guidance, most frequently begins to realize the important part which his own active co-operation can play in determining the date of his release.

Psychotherapy may be said to be applied from the first interview in the institution. We try at this stage to build up a certain feeling of confidence towards the authorities. A complete life-history is prepared shortly after admittance to the institution, a complete psychiatric-neurological examination is carried out, and a genealogical table drawn up. The Danish Marriage Law lays down that any person who is insane, mentally deficient, psychopathic to a serious extent or a chronic alcoholic shall be forbidden to marry without the permission of the Ministry of Justice, provided that such permission may be granted conditionally upon prior sterilization. As early as possible it is important to inform the detainee as to whether he can expect to get permission to marry without prior sterilization. Only a very few express a wish to be sterilized—about 4 or 5 a year.

In the day-to-day treatment we attach great importance to inculcating in the detainee the feeling that he himself is responsible for his future. We therefore make a point of providing opportunities for developing occupational interests such as market gardening, printing, book-binding, joinery, toy-making, and tailoring; all building repairs in the institution are carried out by the detainees. In the half-open department there are opportunities for working in general farming on neighbouring farms, and in the open department there is intensive market gardening with mushroom production as a speciality. The detainees are paid for their work if possible by "piece method". They may use half of their income for tobacco, stamps, books, extra food, and whatever they like.

Because of his psychical abnormalities, which can to some extent be suppressed or corrected, but which very often continue to manifest themselves, the detainee often finds it difficult to hold down a good job in the world outside. It is therefore important that he should be made a diligent worker.

There is besides a lively club life where sport, stamp collecting, chess and bridge, and domestic crafts are widely developed. There is a marionette theatre and a simple stage where classical plays and reviews featuring the daily life of the institution are performed. Education proper is catered for in study circles, and in certain occupations correspondence courses are available.

What I have mentioned so far is perhaps not very different from what may be used in other similar correctional institutions. Perhaps it is elaborated rather differently in Hersted-vester, where the emphasis is always on the psychiatric aspect. As regards direct psychotherapy, however, the working methods differ radically from what is used in a prison or in a hospital. It may be stated, as a fundamental rule, that psychotherapy in general cannot be conducted in the same way in a closed institution as in a private consultation, and especially not if the person in charge of the psychotherapy has a substantial say in the duration of detention. In a few special cases it is of course possible to carry out a regular consultation practice within the scope of the institution, but such cases are always the exception. All too many will feel tempted to exploit such a situation and try to deceive the doctor and themselves. It is a question, above all, of treating not merely the immediate mental symptoms, but also of preventing their recurrence, i.e. to prevent recidivism. The psychotherapy must therefore be carried out in such a way that there is always particular regard to the permanent effect on the patient's personality development. I have already said that, to a large extent, we leave the psychotherapy to the patient himself. This implies, among other things, that we exploit moments of particularly strong emotion and situations when passions are aroused to explain to the detainee his reactions in such situations and so draw analogies with previous, especially criminal, situations in which he has found himself. We call him in, to reason with him and discuss the trouble, and we are often able, from our intimate knowledge of the man's past history, to point out to him the factors which cause him to react in this way. As a rule they come in sooner or later and thank us for our explanations and often tell us that, having thought the matter over, they agree with our interpretation. The time comes when the discussion can be continued so that one is sometimes able to explain to him how he has landed himself in criminal activities in the world outside through such distortions of realities. In other cases, involving fights and so on, as a rule there is a useful opportunity of showing him how to keep his violence under control until a more appropriate occasion for exercising it, when it will not be at the expense of other people; pointing out at the same time that he does not usually behave in this fashion when he is brought before the doctor. It cannot be due merely to the doctor's behaviour, since the doctor often tells him some unpleasant things—things to which his reaction could well be extremely violent.

In a few cases we have applied hypno- or narco-analysis, but in most cases we have confined ourselves to the methods mentioned, partly because just at the present time we are not in a position to go further.

stantially increased scope for the application of psychopath detention treatment. The Danish Criminal Law of 1930 does not resort to the McNaghten rules, but says in section 16 that no person shall be subject to any punishment in respect of any act on his part if, at the time of the deed, he was irresponsible because of insanity or a condition of mind similar thereto or a high degree of mental deficiency.

Section 17, subsection 1, provides for the treatment to be adopted towards any person who, at the moment of perpetration of any crime, was, owing to underdevelopment, weakness or derangement of the mind, including sexual abnormality, in a mental state of a more permanent nature but not of a character for which provision is made in section 16 (above). In cases of this kind the court, after consideration of a medical certificate, in addition to all other relevant circumstances, decides whether the accused can be adjudged as a person who is likely to benefit from punishment.

Subsection 2 provides that in certain cases the sentence may be served in a specially constituted institution, thus originating the so-called psychopath's prison.

Section 70 lays down the course to be followed in cases exempt from punishment under section 16, or in respect of which punishment has been adjudged inappropriate under section 17.

Provision is made, *inter alia*, for admission to mental hospitals, institutions for inebriates, or a "special place of detention" (forvaringsanstalt). The Psychopath Institutions at Herstedvester were brought into use as such special places of detention in 1935. Experience gained in these institutions provides the background for the considerations which follow.

These provisions have so far been used with the greatest caution. In the period 1933-43, the first ten years in which this penal code has been in force, between 1% and 2% of those sentenced were referred for special treatment.

The psychopath institutions in Herstedvester are:

(1) The main one, a detention institution for men, houses about 175 persons. This is the group which is detained on indefinite time.

(2) A corresponding institution for women, appreciably smaller and housing at the present time 13 persons, should have accommodation for 20.

(3) A psychopath prison for men, intended as a general prison, but where the prisoners are under continual surveillance of psychiatrists. In practice it has proved difficult for the courts to determine in advance which criminals should be sent to a psychopath prison, and it is now rarely used and accommodates only 15 persons.

(4) In recent years there has been attached to the institution a special psychiatric observation department which can receive prisoners from all other criminal institutions for observation and treatment. This department can accommodate 35 persons and is officially quite independent of the other departments.

The treatment in this observation department is similar in principle to that given in the main detention institution but suffers from the drawback that the patients are serving a definite time sentence, like the few persons in the psychopath prison who now receive the same treatment as the detainees in the main detention institution. Clinical experience shows that the predetermined term of sentence creates certain difficulties: the need for treatment is less obvious to the patient than when he is serving an indefinite sentence.

The number of inmates in the institutions has grown steadily, and when there was no more room we bought an ordinary farm in a village near Copenhagen and fitted it up as a market garden with accommodation for 20 detainees. These detainees consist partly of castration cases, who are waiting until the effects of castration are sufficiently manifest to justify their release on parole, partly of others who anticipate parole within the near future and of a few older detainees who have made something of a home there.

Later a half-open department was established in an old manor house in South Zealand with accommodation for 40 persons. The small department already mentioned with accommodation for 20 persons is completely open without fencing and locked doors, the detainees working freely in the open fields but keeping within the grounds which comprise only about 6 acres. The department in South Zealand, on the other hand, is surrounded with a light wire fence. There is a permanent night watch, and the detainees work in teams under supervision.

The institution is under the direction of a senior psychiatrist with three assistant psychiatrists and two nurses. A teacher is in charge of the detainees' education and spare time activities, and the library. Welfare work is in the hands of a trained sociologist who has three assistants. The supervising staff are prison officers with special mental hospital training and further training in the institution. The total staff is rather big, nearly one for each two detainees.

The pervading atmosphere and tone of these institutions—determined under purely psychiatric direction—arouses most frequently in the new detainee an immediate awareness that he is in an institution of quite another character than a prison. Later there frequently

Section of Neurology

President—C. WORSTER-DROUGHT, M.D.

[May 27, 1948]

JOINT MEETING WITH THE SOCIÉTÉ DE NEUROLOGIE DE PARIS
AT LA SALPÊTRIÈRE, PARIS

DISCUSSION ON CEREBRAL VASCULAR DISEASE IN THE YOUNG [Summary]

Sir Charles Symonds (*Abstract*): These observations will not include any discussion of migraine or subarachnoid hæmorrhage but will be confined to structural lesions of the brain. In older persons the common causes of a cerebral vascular lesion are hæmorrhage and thrombosis associated with arterial hypertension or atheroma. Hypertension may also occur in the young, but a cerebral vascular lesion in this setting presents no diagnostic problem. Atheroma in the young is so uncommon that it is one of the last causes to be suspected for a cerebral vascular lesion. If the discussion is limited to patients under the age of 35 and without hypertension the problems of ætiology will be of greater interest.

Cerebral embolism from bacterial endocarditis or mitral stenosis is easily recognized, as also cerebral thrombosis from congenital heart disease or syphilitic arteritis. Cerebral hæmorrhage in the young is usually derived from a ruptured aneurysm. Hæmorrhage into an angioma is another cause and may be provoked by minor injury. Two unverified cases of this kind were described with lesions in the brain-stem. Delayed traumatic cerebral hæmorrhage deserves comment. Leukæmia and purpura may also present with cerebral hæmorrhage. Injury to the carotid artery in the neck may cause cerebral embolism; a case was described. Cerebral embolism may also result from compression of the subclavian artery by cervical rib. Fat embolism and air embolism are also of interest.

Disease of the cerebral arteries in the young, apart from syphilis, is rare. The syndromes which result comprise on the one hand the acute hemiplegias, and on the other hand cases in which the symptoms are scattered, progressive or remittent. Polyarteritis nodosa may cause either syndrome. Atheroma in the young may result in cerebral thrombosis; a case was described with post-mortem findings. There are many cases of what appears to be cerebral arterial thrombosis in the young without explanation. The ætiology of these cases was discussed and a case described in which extensive thrombosis of the larger cerebral arteries was found post mortem without arterial disease. Thromboangitis obliterans of the cerebral vessels may also occur, involving either peripheral branches or main trunks. The differential diagnosis of progressive cerebral thrombosis from cerebral tumour is often difficult and may require air pictures. Thrombosis of the intracranial veins causes symptoms which may be divided into those of increased intracranial pressure, which are due to obstruction of venous outflow from the skull; focal epilepsy or paralysis resulting from local congestion; and cranial nerve palsies from compression.

The pathology and mechanism of these syndromes was discussed.

Professor Geoffrey Jefferson: *Intracranial hæmorrhage*.—Intracranial bleeding in the young must be classified first as intra- or extra-cerebral. Much interest has been shown recently in subdural hæmatoma in infancy. I shall consider two different causes, (a) congenital cerebral angiomas, (b) congenital aneurysms, as sources of hæmorrhage.

(a) *Congenital cerebral angiomas* frequently bleed into the subarachnoid space or ventricle giving rise to recurrent attacks of so-called "meningitis". There may have been several such attacks before the diagnosis is arrived at. These angiomas furthermore usually cause epileptic attacks; Jacksonian focal epilepsy in the young

The co-ordination of the direct psychotherapy and the ordinary day-to-day work is most essential and we consider it to be essential to keep the staff informed about the more important happenings. This takes place at weekly meetings where all interested members of the staff have an opportunity of being present, though none is obliged to come.

The detainees are kept informed about the world outside by means of newspapers and wireless. Every detainee may buy himself a crystal set and there is a loud speaker in each assembly room. Finally, what is most important, they can go out. Detainees, who have proved themselves diligent and have conducted themselves well throughout one year, can get permission to go out once a month for eight hours, accompanied by one of the welfare officers in civilian clothes.

Since 1929 Denmark has had a law which permits voluntary castration, subject to permission being obtained from the Ministry of Justice. The law was amended and extended in 1935. Professor Sand (1939) has given an account of the results of the first ten years. A very substantial number of the persons who are sent to the psychopath detention institution because of sexual crime themselves express the wish to undergo the operation, which has long shown itself to be particularly effective. So far, 161 castrations have been performed in the institution. The law admits in theory the possibility of compulsory castration, but this provision has never been used and presumably never will be used. Looking at the question from a psychiatric point of view, I have no doubt whatever that compulsory castration is less beneficial than the voluntary operation. Castration involves in practice a distinct reduction of sexual desire—so great a reduction in fact, that the man who has hitherto been oversexed in relation to his powers of control, or whose sexual needs took an unlawful form for their satisfaction, is able after the operation to steer clear of further criminal activities. Of the 161 cases so far, there have been 4 sexual recidivists, all of whom were homosexuals. None of the cases has relapsed into the more serious crimes, one has been only biologically recidivated (i.e. he has engaged in homosexual activities with adults, which is not punishable in Denmark), but we have naturally taken prompt and serious action in all these cases and retained the recidivist several years before he was again released. Three of them are again released and are doing well, the fourth has recently relapsed.

The physical consequences of castration with adults have proved to be only minor things of no practical importance. In any case they are considerably less striking than those produced by the change of life in women. For psychological reasons glass prostheses are inserted, so that the patient can go to swimming baths and in general can strip before others without arousing attention.

There is no time to go into details about the effects of castration, but I can sum it up by saying that in Denmark we are all agreed that we cannot consider abandoning castration as a method of treatment for sexually abnormal criminals. This unanimity embraces the castrated themselves, who often regret that they have taken so long in deciding to undergo the operation. Time after time they refer to the sense of peace and confidence in their behaviour which follows the operation. Some marry after a time, and there are cases of men who are worried about their inability to give their wives sexual satisfaction, but most are of such an age when they marry that this question is of no great importance. Since we always insist that the woman must be informed about the position before marriage, the matter in the great majority of cases is of no importance.

I would emphasize that the hormonal effects of castration should not be relied upon without some attempt at psychotherapeutic treatment, since I am of the opinion that only in very exceptional cases can we be satisfied with mere castration. As a rule castration cases should be referred for institutional treatment.

As regards the general results of treatment in the institution, we can fairly say that they are promising. We have managed to get the detainees to take part in their own rehabilitation with the necessary enthusiasm.

The detailed elaboration of the material from different points of view is not yet completed, but we can say that more than 50% of the detainees after some years go back to normal life in the community.

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case of necrosis of the anterior pituitary gland following collapse in childbirth in which the veins in the pituitary stalk were found to be thrombosed; and to a case in which the rupture of an aneurysm in the cavernous sinus was followed by thrombosis of the cavernous sinus on both sides and their connecting sinuses.

In two cases of venous hæmangioma of the pons (with anatomical findings) the clinical features were in many ways similar to those of disseminated sclerosis.

[May 28, 1948]

JOINT MEETING WITH THE SOCIÉTÉ DE NEUROLOGIE DE PARIS
AT L'HÔPITAL STE. ANNE, PARIS

DISCUSSION ON INTRACRANIAL HYPOTENSION [Abstract]

Dr. P. Puech: *I. Introduction.*—Intracranial hypotension comes into the framework of disturbances of cerebromeningeal hydrodynamics, that is, it is one of the hydraulic reactions of the brain and its envelopes to the most diverse processes: a vast chapter in general and nervous pathology.

Professor Leriche will show how, while studying the clinical manifestations formerly attributed to post-traumatic intra-cranial hypertension, he was led to identify hypotension.

Following this, Doctors P. Puech, P. Guilly, J. Morice and M. Brun will consider the principal forms of hypotension, some of which are associated with other disturbances of cerebromeningeal hydrodynamics. Their discussion will be based on 238 cases of hypotension, confirmed at operation.

Finally, Professor Petit-Dutaillis, with Doctor G. Guiot, will describe the therapeutic indications in hypotension.

Professor R. Leriche: *II. Post-traumatic hypotension of the cerebrospinal fluid.*—The existence of hypotension was established in 1915–16 as a result of the following observations in minor head wounds and in trephined patients with depressed scars:

- (1) Hypotension shown by the manometer after lumbar puncture.
- (2) Restoration of pressure by subcutaneous or intravenous injections of artificial serum.
- (3) Disappearance of headache and other symptoms at the same time, with
- (4) Bulging of the depressed scars.

A little later, in 1920, it was observed in closed fractures of the skull that hypotension might develop primarily or secondarily as well as hypertension, and with almost identical symptoms which disappeared immediately after the intravenous injection of 40 c.c. of distilled water. This led to the interpretation of the symptoms of fracture of the petrous portion of the temporal bone or of the lamina cribrosa with loss of fluid as being due to hypotension. The injection of distilled water caused all the symptoms (coma, hyperthermia, slow pulse) to disappear at the same time as fluid escaped in jets through the ear or nose. Similar observations were made in Jacksonian epilepsy during fits, when hypotension is perhaps as frequent as hypertension.

During the same period it was observed that secondary fistulization of the ventricle after the removal of splinters in the brain, followed by abundant loss of fluid, was accompanied by hyperthermia (39–40° C.), cyanosis and peripheral coldness. The intravenous injection of distilled water caused all the symptoms to disappear in a few moments.

An analysis of what had been seen (collapse of the walls of the ventricle) led to the supposition that in severe hypotension there was a disturbance of ventricular form, a collapse which affected the function of the vegetative centres.

This hypothesis fitted a case which had been observed in 1915, of great loss of ventricular tissue, with coma and hyperthermia. Filling of the ventricle with an iodoform paste liquefied by heat had brought about a temporary recovery of the

is not infrequently due to cortical angiomas. Although they may bleed they do not cause cranial nerve palsies nor very often intracerebral bleeding, though they can do so. Surgical treatment does little good unless the angioma is small.

(b) *Congenital aneurysms*.—These are much commoner than angiomas. My youngest patient was 9 months old. There are three possible ways in which a congenital aneurysm can show itself, (1) by subarachnoid leakage, (2) by compressing the second, third, fourth or (rarely) other cranial nerves, and (3) by intracerebral bleeding. I have almost exhausted my interest in (1) and (2) having seen a great number, but I have found a new interest in intracerebral bleeding, which is the especial feature of aneurysms of the anterior and middle cerebral arteries. In some instances in which a bloody fluid is found on lumbar puncture the blood has arrived there by the intraventricular route: this is especially true of anterior cerebral aneurysms. Stupor is a sign of intracerebral and *scarcely at all* of purely subarachnoid bleeding. Surgical treatment is sometimes possible.

Dr. J. Purdon Martin: In addition to arterial hæmorrhage, thrombosis and embolism we must think of venous hæmorrhage, venous thrombosis and venous embolism; I shall also refer to some cases of venous hæmangioma. Venous thrombosis is much the most common of these conditions; venous hæmorrhage is frequently secondary to venous thrombosis and the cases in which it occurs independently are usually traumatic; venous embolism (if it occurs) may be one cause of venous thrombosis. The most important groups of cases of venous lesions are:

(a) Those occurring in association with childbirth. (b) Those occurring in young children. (c) Those due to trauma.

(a) In the cases that are associated with childbirth thrombosed veins are found on the surface of the brain and blood clot may be found in the superior longitudinal sinus, or other of the cranial sinuses. At our Meeting in London last year Dr. Garcin described a most interesting case in which the straight sinus and the great veins of Galen were thrombosed. The thrombosis of the veins is associated with an effusion of blood on the surface of the brain, with discrete hæmorrhages into its substance extending to a variable depth and with a variable degree of softening. Subsequently gliosis occurs in the affected area and a depressed scar is left on the surface of the brain. The usual clinical history comprises convulsions of sudden onset, hemiplegia and, eventually, good functional recovery. The cause of the thrombosis in these cases is still unknown, but the possibility of embolism from the veins of the pelvis, or of the lower limbs, must be closely considered. Some embolic material, e.g. a bubble of air, might pass either by way of the right auricle and jugular veins, or by way of the vertebral veins, but it is doubtful whether the former route could be traversed by a solid embolus, since it would be more likely to be diverted into the lungs.

(b) Cases of venous embolism in young children seldom come to autopsy, but a number have been confirmed, e.g. two cases associated with heart disease described a number of years ago by Lhermitte and his co-workers, and studies have also been made by others. The pathological anatomy and the clinical features of these cases in children are very similar to those in the cases already referred to. It is possible that the condition of lobar sclerosis found in later life in subjects of infantile hemiplegia is a consequence of thrombosis of veins with hæmorrhage and subsequent gliosis.

(c) The traumatic cases are of different types. Thrombosis of the superior longitudinal sinus consequent upon superficial gunshot wounds of the brain and its clinical features were described by Holmes and Sargent, and in rare instances a similar syndrome may result in cases of closed head injury. It is now generally agreed that chronic subdural hæmatoma results from venous hæmorrhage and there are cases of subarachnoid hæmorrhage following trauma (with or without concussion) in which the bleeding is probably of venous origin.

As special instances of venous thrombosis (confirmed by autopsy) I will refer to a

are described. Sometimes the patients are in a state of coma with perhaps hemiplegia, or status epilepticus. These appearances often lead to a diagnosis of softening of the brain or of cerebral hæmorrhage. Again the patient may show from the first hemiplegia, monoplegia, oculomotor paralysis. Yet again, he may be brought in because of local or generalized convulsions. Hypothalamic symptoms are the rule. If they are accentuated a true hypothalamic form is seen.

Mental type.—Cases of the principal forms of mental disease due to hypotension are also reported. We have described a form of the depressive melancholic type, a form of the confusional type, forms with manic attacks and narcoleptic forms. Thiébaud and Daum (1945) have isolated a form resembling general paralysis. We have also observed forms producing states of a schizophrenic type. For some years Professor Delay has stressed the effect of "cerebral pneumotherapy" in intracranial hypotension, but he also emphasizes its important action on the intellectual and the emotional sphere.

Modes of progression.—The condition of intracranial hypotension may be acute or chronic, but in either case the course generally follows a definite pattern. The prodromal period, which may last from a few days to several months, is characterized by headache, loss of weight, emotional changes and often diabetes insipidus. The symptoms of this stage are often recognized only retrospectively, in the established phase, when the serious nervous and mental symptoms have appeared. These may develop insidiously or suddenly, after a severe attack of headache, often fronto-temporal resembling facial neuralgia. Questioning then reveals the fact that the earliest symptoms occurred mainly in the morning, appeared a long time after meals and were relieved by taking food or drink and by lying with the head low. If "re-inflation of the ventricles" is not carried out as an urgent measure the patient falls into coma and dies. In other cases the hypotensive syndrome lasts for months or years in the chronic state, and the diagnosis is mistaken until the day when ventricular puncture reveals the "ventricular collapse" of Clovis Vincent.

Anatomical forms.—Both isolated and associated forms of intracranial hypotension exist. The diagnosis is again difficult, but it is always made clear by trephine puncture of the ventricle, which is also the first stage of treatment.

Isolated intracranial hypotension.—There were 135 cases, of which 24 were post-traumatic, 25 were post-operative, 19 were secondary to various diseases, and 67 were apparently primary.

Whatever its cause may be, isolated hypotension shows all the clinical and evolutionary characteristics already described. The neurosurgeon observes that the dura mater does not pulsate; when this membrane is incised, the brain is seen to be shrunken, collapsed and pulseless. This state of cerebral dehydration is confirmed by ventricular puncture. No fluid escapes when the trocar penetrates it, and one hears the sound of air being sucked into the ventricle. If any ventricular fluid is found, it cannot be removed except by aspiration or by swinging the head backwards or compressing the jugular veins.

Hypotension associated with other disturbances of cerebromeningeal hydrodynamics.—There were 71 cases, of which 16 were post-traumatic, 46 secondary and 9 apparently primary.

It often happens that hypotension verified by trephine puncture is, nevertheless, associated with (1) a certain amount of more or less diffuse cerebral œdema (gelatinous, grey, hypotensive brain); or (2) ventricular dilatation in spite of hypotension of the fluid; or (3) serous meningitis or subdural hydroma with hypotension.

The cerebral mass and the space it occupies in the cranial casing are sufficient to make it easy to realize the possibility of such associations, which we have confirmed at operation. Any one of the disturbances of cerebromeningeal hydrodynamics may be primary or secondary. It has seemed to us that the so-called localizing symptoms were related sometimes to cerebral collapse, especially marked in the

vegetative functions and of consciousness. There was therefore reason to attach great importance to ventricular form in the interpretation of the symptoms. The observed facts, as a whole, made it possible in 1922 to relate hypotension to three conditions:

(1) Loss of fluid into the soft parts (lumbar puncture in which the hole leaks, resulting in headaches) or to the outside (fractures of the petrous bone, ventricular fistula, operative losses).

(2) Insufficiency of dialysis in the choroid plexus as a result of acute or chronic vasomotor disturbances (closed fracture of the skull with vaso-constriction in the basal arteries—surgical shock) or inflammation or sclerosis.

(3) Enlargement of the subarachnoid spaces in patients trephined in the past.

The symptoms resemble those of hypertension—but less marked—and those of meningism. The hyperthermia of severe cases suggests infection. In minor cases (after lumbar puncture in Jacksonian epilepsy) headache and vertigo occur.

Treatment has consisted in intravenous injections of 40–50 c.c. of distilled water. The results have been striking. For chronic cases resembling those described by Puech in 1942 the following have been suggested: ligation of the inferior longitudinal sinus, ligation of the internal jugular vein, and peri-carotid sympathectomy. This last has been done four times. It causes cranio-cerebral hyperæmia seen in the fundus of the eye, and makes depressed scars bulge. Patients were doing well after one year, and one patient was followed up for 20 years.

Drs. P. Puech, P. Guilly, J. Morice and M. Brun: *III. The principal forms of intracranial hypotension.*—Professor Leriche has just described how, having isolated intracranial hypotension, he determined its morbid physiology and treatment.

[The literature of the subject was then reviewed.]

According to our statistics, verified intracranial hypotension represents 7.2% of all cases of cerebral neurosurgery. In a series of 3,284 intracranial affections operated upon in the Neurosurgical Department of the Hôpital Sainte-Anne there were 238 cases of hypotension which were verified by trephine puncture or by direct exploration of the brain. We have not included cases diagnosed by lumbar or sub-occipital puncture, as these methods quite often give a poor idea of what is happening in the ventricles, and the conception of a uniformly lowered pressure in the cerebro-spinal system as a whole is an over-simplification and must be revised.

We are therefore considering mainly the neurosurgical forms of intracranial hypotension which justify “re-inflation of the ventricles”.

The abortive forms which recover after “cerebromeningeal rehydration” are much more frequent than our statistics show.

In this series of 238 cases of intracranial hypotension 68 per cent. were secondary (18.8% followed accidental trauma, 10.5% were post-operative complications and 38.7% were secondary to a medical or surgical disease), and 32% apparently primary. This means that sometimes the physician and sometimes the surgeon must anticipate and prevent or detect and treat intracranial hypotension. The clinical diagnosis is often difficult, but must be considered on many occasions.

Clinical forms.—Intracranial hypotension, related to more or less acute cerebro-meningeal dehydration, can produce symptoms like those of intracranial hypertension. In both, the patients complain of headache and vomiting; there may be undoubted papillœdema, at least in our experience, though we are aware that certain authors have stated that the disc remains normal in hypotension. The electroencephalogram may show diffuse or more localized changes in either condition.

We have stressed the three main clinical aspects of intracranial hypotension: the neurological, the psychiatric and the neuropsychiatric which are about equally frequent.

Neurological type.—Typical cases showing the principal neurological symptoms

are described. Sometimes the patients are in a state of coma with perhaps hemiplegia, or status epilepticus. These appearances often lead to a diagnosis of softening of the brain or of cerebral hæmorrhage. Again the patient may show from the first hemiplegia, monoplegia, oculomotor paralysis. Yet again, he may be brought in because of local or generalized convulsions. Hypothalamic symptoms are the rule. If they are accentuated a true hypothalamic form is seen.

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region corresponding to the localizing signs, and sometimes to local serous meningitis or local cerebral œdema associated with the hypotension.

These forms should be distinguished from cerebral collapse related to direct compression of the brain, which is accompanied by intracranial hypertension. The compression may be due to a subdural hæmatoma or to predominant serous meningitis. Hypotension occurs only if the hæmatoma has been evacuated or the serous meningitis drained.

It must be noted that the various hydraulic disturbances of the cerebromeningeal system (cerebral œdema, serous meningitis, ventricular hydrocephalus, cerebromeningeal dehydration) may not only be combined, but may follow each other in the same patient. This may be a fortunate or normal event, or, on the contrary, a grave, and very often fatal, complication. In either case, the degree of disturbance shown by the electroencephalogram is of indisputable prognostic value.

If a fatal issue is feared, it is of the highest importance to recognize the dominant disturbance so that it may be suitably treated. Drainage for serous meningitis, dehydration for œdema, and restoration of the ventricular balance for hydrocephalus may follow each other or be combined in one and the same case.

Hypotension associated with other intracranial lesions.—The lesions may be post-traumatic or non-traumatic. They may be diffuse or local, tumoral, vascular, atrophic or infectious. All may be accompanied by other disturbances of cerebromeningeal hydrodynamics. J. Lebeau (1947) has shown that temporal hernia may be associated with intracranial hypotension and hypertension. In every case the primary lesion must be treated first, and the hydrodynamic disturbance dealt with afterwards if necessary.

Causes.—The cause of hypotension is sometimes obvious, but often very difficult to detect. There are secondary forms and clinically primary forms.

A study of the patient's history, clinical investigation, a search for the biological signs of hypotension, and especially a systematic study of the ventricular fluid, which often shows ventricular hæmorrhage, hyper-albuminosis and sometimes, on the contrary, a predominant leucocytic reaction, a comparison of the fluid of serous meningitis and of the ventricular fluid, and a complete humoral examination often give useful information.

The authors then dealt with:

- (1) *Post-traumatic hypotension*, on the basis of 45 cases. Recent and late forms, with or without leakage of fluid to the outside or into the subdural space.
- (2) *Post-operative hypotension*, on the basis of 25 cases.
- (3) *Secondary hypotension*, after many surgical or medical affections, on the basis of 87 cases.
- (4) *Therapeutic hypotension*, following radiotherapy (Stuhl, Bordet and Thiébaud, 1938) or drug therapy, on the basis of 5 cases.
- (5) *Clinically primary hypotension*, on the basis of 76 cases.

The type of hypotension which follows lumbar puncture, spinal anæsthesia, ventricular puncture or drainage of the ventricles in hydrocephalus is well known and will not be considered except to mention that hypotension left to itself is often the immediate cause of death in diverse conditions (traumatic, operative, circulatory, infectious, toxic or due to malnutrition). The surgeon is sometimes able to avoid this occurrence, and also secondary hæmorrhage or secondary softening of the brain. We have had the opportunity of observing a certain number of patients showing the classical symptoms of cerebral apoplexy in whom we have been able to prevent the hæmatoma by re-establishing the disturbed balance of the cerebrospinal circulation.

Morbid physiology.—This is easy to conceive. There may be a leakage of fluid, defective secretion or excessive absorption. Schaltenbrand and Wolf have tabulated it thus: "Hypotension of the cerebrospinal fluid may be due either to diminished

secretion of fluid with constant absorption, or to increased absorption with constant secretion. These disturbances may occur:

- (1) If the flow of blood towards the plexus is diminished or interrupted.
- (2) If the secretion of the plexus is diminished by nervous influences.
- (3) If lesions in the cells of the plexus prevent the secretion of cerebrospinal fluid.

The absorption of cerebrospinal fluid may be increased if: (a) The cerebrospinal fluid goes elsewhere—perforation of the dura mater. (b) The osmotic pressure of the blood increases and allows the cerebrospinal fluid to enter the blood stream."

We would point out that the problem of intracranial hypotension is a special case in the problem of water metabolism in the tissues and is related to that of œdema. It is well known that this is at present the object of very active research and we refer the reader to the work of Mach on states of dehydration, in which the still very incomplete data collected so far are summed up. This problem is further complicated in that we are dealing with the brain working in its rigid cranial casing. Reversible and irreversible forms of hypotension exist, such as the recurrent and finally incurable forms connected with atrophic lesions of the choroid plexuses.

In the patients we are considering, where death seems imminent, direct action on disturbances of the blood circulation (cardiovascular drugs, sympathetic surgery) are of little use, even if these disturbances are primary. On the other hand, neurosurgical procedures designed to restore the water balance of the brain and its envelopes directly are often efficacious. These operations, which first of all constitute urgent neurosurgery, act, in their turn, on the disturbances of the blood circulation.

238 cases of serious intracranial hypotension were operated upon with 43 deaths (18%). There are practically no sequelæ in isolated hypotension; these only occur after combined forms.

Professor D. Petit-Dutaillis and Dr. G. Guiot: IV. Therapeutic indications in intracranial hypotension.—The therapeutic indications are dominated by three considerations: the variable difficulties of diagnosis, the facts observed on direct examination of the brain and on exploration of the ventricles, and the possibility that intracranial hypotension and hypertension may alternate or succeed each other in the same patient.

The diagnosis cannot be established without complementary investigations. For a long time it was believed that the diagnosis could be based on a single spinal manometric test. This may be sufficient in conditions due for instance to lumbar puncture in patients not suspected of tumoral diseases, complications of spinal anaesthesia, hypotension in patients trephined in the past. But in head injuries, or in the interpretation of post-operative complications in neurosurgery, this method only leads to serious diagnostic and therapeutic mistakes.

In neurosurgery, it is above all the exploration of the brain through simple trephine holes, and the results of puncture of the ventricles, which allow the diagnosis of intracranial hypotension to be clearly established.

The chief fact is the diminution of the volume of the brain as a result of complete or relative emptiness of the ventricles (ventricular collapse of Clovis Vincent). In pure cases this collapse is bilateral and symmetrical, but it may be unilateral especially in forms of traumatic origin. This unilateral collapse may be associated with some aspects of serous meningitis, especially with a subdural sheet of fluid on the same side. The other hemisphere may be normal or changed (serous meningitis, mild œdema, atypical forms of intracranial hypotension according to Puech). In the pure forms, injection of fluid or air into the ventricles is enough to restore the brain to its original volume and to make all the symptoms disappear. In other cases, though the consistency may be normal, the brain does not remain filled, because of a leak in the pools at the base of the brain. In the most serious cases, the collapse of the walls of the ventricles is accompanied by disturbances of the cerebral tissues, which have lost all their elasticity and the flaccid brain allows the fluid to leak out through

region corresponding to the localizing signs, and sometimes to local serous meningitis or local cerebral œdema associated with the hypotension.

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Section of Urology

President—WALTER W. GALBRAITH, M.B., F.R.F.P.S.

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Urethrostomy Drainage of the Bladder? ¹

By JOHN G. SANDREY, F.R.C.S.

URETHROSTOMY drainage of the bladder has been carried out for many years at Saint Peter's Hospital in the treatment of urethral stricture. Harrison (1878) recommended the introduction of a tube along the posterior urethra to drain the bladder after external urethrotomy or perineal section as a means of preventing post-operative febrile reactions. It was not until 1885, however, that Harrison described the operation of combined internal and external urethrotomy with urethrostomy drainage with which his name is now associated. Originally recommended for "impassable or very extensive strictures which will not dilate" the operation was also used in "cases of peri-urethral abscess, fistula or extravasation" and eventually came to be employed exclusively in the latter group. The value of combined perineal drainage of both the bladder and the subcutaneous tissues in cases of stricture complicated by gangrenous cellulitis ("perineal phlegmon") was emphasised by both Freyer and Thomson-Walker in their writings and it is, I believe, still to be regarded as the method of choice in these cases, for, in addition to providing for the direct escape of urine from the bladder by the most dependent route, it avoids opening up fresh planes of cellular tissue. Most of us have looked on helplessly while a spreading gangrenous cellulitis of the abdominal wall or a gas-infection has developed after suprapubic cystostomy in cases of this kind, yet how easily this could have been prevented by drainage from below! Fortunately the so-called perineal phlegmon is becoming less common nowadays but in the half-dozen cases I have treated by combined perineal section and urethrostomy in the past few years it has always been very gratifying to watch the rapid recovery of patients who, as a rule, when admitted to hospital exhibited all the signs of the profound toxæmia so characteristic of this form of urinary suppuration. Furthermore, the infection both in the urinary tract and the cellular tissues has cleared up rapidly and completely, and incidentally the divided stricture has become more amenable to dilatation afterwards.

Apart from its occasional use in urethral stricture urethrostomy drainage of the bladder has never been popular with urologists in this country although it appears to have been extensively used for a long time in the United States. Young and his associates (1926) recommended this procedure for diverting the urine when operating for hypospadias and other deformities of the penis and I believe the majority of British plastic surgeons now follow this example. Young (1934), discussing the treatment of the obstructed bladder, advised the substitution of the urethral catheter for suprapubic drainage because of the high mortality of the latter. Where the urethra did not tolerate a catheter well, however, he also

¹This paper will appear *in extenso* in the *Post-Graduate Medical Journal*. The author discusses first, those methods of bladder drainage now in common use, secondly, personal experiences of drainage of the bladder by urethrostomy and lastly he evaluates the various procedures in order to determine under what circumstances they should be employed. The present paper deals with urethrostomy drainage of the bladder.

the trephine holes. The pathogenesis of these tissue changes is still under discussion.

The treatment may aim at direct replacement of the missing fluid (intravenous injections of distilled water, massive injections of serum repeated as required). Treatment with drugs capable of acting on the arterial blood-pressure, the capillary permeability or the secretion of the plexuses (perfusion of adrenaline or ephedrine in physiological or hypotonic serum, syncortil, pitressin). Some authors have recommended vitamin P.

Air can be injected into the ventricles. The quantity of air varies, and it must be injected prudently, until the ventricles are "reinflated". This air has a twofold action: it re-establishes the intraventricular pressure, and it causes irritation of the choroid plexuses, which tends to re-establish secretion.

In severe cases direct replacement of the fluid mass by injecting physiological serum or, better, Ringer's solution into the ventricles is the method of choice because of its rapid effect. In severe cases of collapse of the ventricles which do not respond to this treatment, the indirect methods are indicated, combined with the Trendelenburg position. This favours blood stasis, and, by relieving the nuclei at the base of the brain, sometimes gives better results than one dares to hope for.

Finally, the prevention of hypotension is most important to neurosurgeons. Repletion of the ventricles is a wise practice at the end of operations to prevent passive collapse (compression by a hæmatoma or a tumour), and also after operations on the posterior fossa to restore a normal cerebrospinal fluid pressure. All operations, even those on the nerve roots or the spinal cord, demand a reduction in the loss of cerebrospinal fluid during operation, and its replacement in order to simplify the immediate post-operative course.

Dr. W. Ritchie Russell: During the late war the British neurosurgeons came to recognize what they call a *low-pressure state* which seems to be identical with *l'hypotension intra-crânienne*. We are now more aware of this condition, but it must be admitted that our conceptions with regard to it are somewhat vague.

Patients who, after operation or injury, develop unexplained coma are suspected of developing this low-pressure state, and if on lumbar puncture or exploratory trephine the pressure is low, treatment is instituted to raise the intracranial pressure—the foot of the bed is raised and fluids are forced. This treatment is also followed in cases of subdural hæmatoma where, after operation, the brain remains retracted and the patient drowsy. The patient's condition usually improves, but why? Are these patients just suffering from water depletion or does intracranial hypotension cause coma by some mechanical displacement of the brain? Cases also occur of negative intracranial pressure in which there is no obvious disturbance of cerebral function.

With regard to intracranial hypotension following injury the position is complex. There is no doubt that in many cases of prolonged post-traumatic stupor a stage develops in which the intracranial pressure may become very low or even negative so that on exploratory trephine the brain falls away when the dura is opened. These cases are often severely dehydrated and the difficulty is to assess how much of the patient's coma is due to water depletion and how much to some other factor. Further, is the dehydration the result merely of inadequate fluid intake or of a biochemical disorder due to hypothalamic dysfunction? The hypothalamus and pituitary mechanisms control water metabolism to a profound extent. It seems possible and indeed probable that this mechanism should sometimes become disordered by trauma. I feel that the mechanism underlying intracranial hypotension can perhaps be unravelled by detailed biochemical studies.

Section of Urology

President—WALTER W. GALBRAITH, M.B., F.R.F.P.S.

(May 27, 1948)

Urethrostomy Drainage of the Bladder? ¹

By JOHN G. SANDREY, F.R.C.S.

URETHROSTOMY drainage of the bladder has been carried out for many years at Saint Peter's Hospital in the treatment of urethral stricture. Harrison (1878) recommended the introduction of a tube along the posterior urethra to drain the bladder after external urethrotomy or perineal section as a means of preventing post-operative febrile reactions. It was not until 1885, however, that Harrison described the operation of combined internal and external urethrotomy with urethrostomy drainage with which his name is now associated. Originally recommended for "impassable or very extensive strictures which will not dilate" the operation was also used in "cases of peri-urethral abscess, fistula or extravasation" and eventually came to be employed exclusively in the latter group. The value of combined perineal drainage of both the bladder and the subcutaneous tissues in cases of stricture complicated by gangrenous cellulitis ("perineal phlegmon") was emphasised by both Freyer and Thomson-Walker in their writings and it is, I believe, still to be regarded as the method of choice in these cases, for, in addition to providing for the direct escape of urine from the bladder by the most dependent route, it avoids opening up fresh planes of cellular tissue. Most of us have looked on helplessly while a spreading gangrenous cellulitis of the abdominal wall or a gas-infection has developed after suprapubic cystostomy in cases of this kind, yet how easily this could have been prevented by drainage from below! Fortunately the so-called perineal phlegmon is becoming less common nowadays but in the half-dozen cases I have treated by combined perineal section and urethrostomy in the past few years it has always been very gratifying to watch the rapid recovery of patients who, as a rule, when admitted to hospital exhibited all the signs of the profound toxæmia so characteristic of this form of urinary suppuration. Furthermore, the infection both in the urinary tract and the cellular tissues has cleared up rapidly and completely, and incidentally the divided stricture has become more amenable to dilatation afterwards.

Apart from its occasional use in urethral stricture urethrostomy drainage of the bladder has never been popular with urologists in this country although it appears to have been extensively used for a long time in the United States. Young and his associates (1926) recommended this procedure for diverting the urine when operating for hypospadias and other deformities of the penis and I believe the majority of British plastic surgeons now follow this example. Young (1934), discussing the treatment of the obstructed bladder, advised the substitution of the urethral catheter for suprapubic drainage because of the high mortality of the latter. Where the urethra did not tolerate a catheter well, however, he also

¹This paper will appear *in extenso* in the *Post-Graduate Medical Journal*. The author discusses first, those methods of bladder drainage now in common use, secondly, personal experiences of drainage of the bladder by urethrostomy and lastly he evaluates the various procedures in order to determine under what circumstances they should be employed. The present paper deals with urethrostomy drainage of the bladder.

the trephine holes. The pathogenesis of these tissue changes is still under discussion.

The treatment may aim at direct replacement of the missing fluid (intravenous injections of distilled water, massive injections of serum repeated as required). Treatment with drugs capable of acting on the arterial blood-pressure, the capillary permeability or the secretion of the plexuses (perfusion of adrenaline or ephedrine in physiological or hypotonic serum, syncortil, pitressin). Some authors have recommended vitamin P.

Air can be injected into the ventricles. The quantity of air varies, and it must be injected prudently, until the ventricles are "reinflated". This air has a twofold action: it re-establishes the intraventricular pressure, and it causes irritation of the choroid plexuses, which tends to re-establish secretion.

In severe cases direct replacement of the fluid mass by injecting physiological serum or, better, Ringer's solution into the ventricles is the method of choice because of its rapid effect. In severe cases of collapse of the ventricles which do not respond to this treatment, the indirect methods are indicated, combined with the Trendelenburg position. This favours blood stasis, and, by relieving the nuclei at the base of the brain, sometimes gives better results than one dares to hope for.

Finally, the prevention of hypotension is most important to neurosurgeons. Repletion of the ventricles is a wise practice at the end of operations to prevent passive collapse (compression by a hæmatoma or a tumour), and also after operations on the posterior fossa to restore a normal cerebrospinal fluid pressure. All operations, even those on the nerve roots or the spinal cord, demand a reduction in the loss of cerebrospinal fluid during operation, and its replacement in order to simplify the immediate post-operative course.

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advised that there should be no delay in establishing urethrostomy drainage. Barney (1934) described the very simple method of performing urethrostomy with catheter and clamp which he had used for many years. Lewis (1943) advocated urethrostomy for drainage of the paralysed bladder and claimed that there was less leakage, less infection, better drainage, in fact many advantages over other methods.

Dissatisfaction with routine methods of bladder drainage by cystostomy or urethral catheter first led me to explore the possibilities of urethrostomy for this purpose early in 1946 and during the past two years I have employed it more or less exclusively, the series of cases now totalling 379.

The following table shows the various conditions treated by urethrostomy drainage:

Temporary or pre-operative bladder drainage	58 cases
Post-operative drainage	
(a) Prostatectomy, one stage (retropubic, Freyer, vesico-capsular)	157 cases
(b) Prostatectomy, after suprapubic drainage	55 cases
(c) Prostatectomy, after urethrostomy drainage	49 cases
(d) Perurethral resection	8 cases
(e) Diverticulectomy	24 cases
(f) Operations for carcinoma of the bladder (open diathermy, partial cystectomy)	16 cases
(g) Miscellaneous (excision stricture penile urethra, perineal phlegmon, calculus, &c.)	12 cases
Total	379 cases

The method used in the majority of the cases was that described by Barney and will be subsequently referred to as the "closed" method. A rubber catheter is passed along the urethra to its full length and the distal end securely clamped with a curved artery forceps (Moynihan or curved Spencer Wells pattern). The forceps is advanced until its beak reaches the bulbous urethra and by rotating the handle through 180 degrees the point is made to present in the perineum where it is cut down on. The end of the catheter is disengaged from the forceps and the instrument withdrawn through the incision to the correct length for bladder-drainage. This method is speedy, simple and requires no special equipment or gadgets. In very ill patients it can readily be performed in bed under local anaesthesia. In that group of cases (comprising about 20%) where the external meatus is stenosed or the urethra congenitally small the "open" method has been employed. An incision is made in the perineum on the curve of a small metal bougie dividing the skin, fascia, bulbocavernosus muscle, the spongy tissue and the urethral mucosa. The edges of the latter must be carefully identified and grasped with fine tissue forceps before attempting to pass the catheter, otherwise the urethra will tend to invaginate and prevent the passage of the instrument. The open is much more difficult than the closed method of urethrostomy as it requires wider dissection in an extremely vascular area. It should not be attempted under local anaesthesia.

The best position for the urethrostomy opening has been found to be in the scrotal raphe about one inch in front of the perineo-scrotal angle. The site of this opening is a matter of some importance. If placed too far back it is less accessible for nursing, contamination from the anus more readily occurs, kinking of the tube by the weight of the scrotal contents is hard to avoid and spontaneous closure of the fistula after removal of the catheter is slower. If too far forward the catheter tends to kink excessively at the subpubic angle and if it should come out replacement may be difficult.

Transfixion of the catheter was found to be unsatisfactory mainly because of leakage from the stitch-hole in the rubber and the best method of fixation so far devised has been by numerous half-hitches around the catheter and stitched to the skin in front and rear. Silk, nylon or any other non-absorbable suture material serves equally well.

For post-operative drainage after prostatectomy, partial cystectomy, &c., a whistle-tip resectoscope catheter with at least three lateral eyes has been found to be the most satisfactory. The perineal urethra will readily accommodate 22 and 24 Ch. sizes and when hæmorrhage was not well controlled size 26 Ch. has been used on several occasions. In three cases urethrostomy has been combined with suprapubic drainage and drip-irrigation when severe hæmorrhage had occurred after Freyer prostatectomy; as an alternative to the latter method of combined drip irrigation, a Foley type of catheter was introduced by open urethrostomy on one occasion and control of bleeding was complete.

The best position for nursing the patient seems to be with the tube draining over the thigh and the scrotum supported by means of an elastoplast bridge.

The chief disadvantages of this method are as follows:

First, a scrotal hæmatoma may form. This does not appear to be a matter for great concern

as rapid absorption without any tendency to infection has been the rule in all the cases observed.

Secondly, replacement of the urethrostomy tube may be difficult, especially if the attempt is delayed for more than a few hours. An opening made too far forward will further increase the difficulties of replacement.

Thirdly, slight incontinence of urine is not uncommon, especially after prolonged drainage with the larger sizes of catheters. This is never severe and full control normally returns within a few weeks. No case of permanent incontinence has been observed.

Finally, leakage of urine from the resulting perineal fistula after removal of the tube will occur with each act of micturition. This is, of course, normally under voluntary control. It ceases, in the average case, after four or five days but may persist longer if the opening has been made too far back in the perineum or if circumstances have made it impossible to get the patient out of bed immediately after removal of the tube. (In one of my cases after prostatectomy severe hæmatemesis from a duodenal ulcer necessitated three months' treatment in bed. On getting the patient up at the end of this time the perineal fistula, which had leaked intermittently all this time, closed spontaneously within a few days.) In the erect posture the weight of the scrotal contents tends to drag the external opening away from the urethra and this will accelerate the obliteration of the track. In none of my own cases has spontaneous closure of the fistula failed to occur. Leakage is undoubtedly the chief disadvantage of urethrostomy drainage but it is, after all, a small price to pay for the added safety the method confers on "closed" operations on the bladder. Unlike the leakage associated with suprapubic cystostomy it is, however, under voluntary control. It is always necessary to warn patients of leakage before removing a perineal tube and to reassure them that this will only be a temporary state of affairs, otherwise they are apt to assume that some mishap has befallen them.

Most of the advantages of urethrostomy, especially the simplicity of the procedure, have already been emphasized. Compared with suprapubic cystostomy the outstanding feature is the difference between dependent and uphill drainage and, in bladder obstructions, the striking contrast between the mortality rates of the two methods. Other features favouring urethrostomy are: first, an intact abdominal wall after pre-operative drainage instead of an infected abdominal tube track, so that a subsequent suprapubic operation is safer, easier and cleaner; secondly, post-operative drainage of the bladder is away from the suture line and allows complete closure in most instances. Compared with catheter drainage the main advantage is the avoidance of most of the ill-effects of urethritis by excluding nearly two-thirds of the entire urethra; furthermore, there is always adequate provision for free drainage alongside the perineal catheter. In addition, the larger sizes of catheter, better methods of fixation, elimination of the distal (pre-pubic) bend of the urethra, the abolition of any time-limit, are all factors which make urethrostomy preferable to catheter drainage with the possible exception of that small group of cases where the external meatus is large and where drainage will probably not be required for longer than seven to ten days. While it can be said that a stricture will almost invariably follow incision of the penile urethra it can be stated, equally dogmatically, that this complication is unlikely to occur in the perineal urethra unless the entire circumference has been divided and the ends separated. In one patient incision of the bulbous urethra for the removal of recurrent calculi revealed no tendency to contracture in spite of three previous urethrolithotomies at the same site.

SUMMARY AND CONCLUSIONS

(1) Suprapubic cystostomy offers no real solution to the relief of bladder obstructions because, in the first place, it is mechanically unsound and will always be associated with a high incidence of fatal urinary infections; secondly, permanent suprapubic drainage is worse than a sentence of death to most individuals and almost any operative risk is justified in avoiding it. In the treatment of the paralysed bladder, however, suprapubic drainage appears to be still the safest and most satisfactory method for routine use.

(2) Having regard to the severe effects of traumatic urethritis, both immediate and late, the indiscriminate use of the tied-in catheter to drain the bladder for periods exceeding two or three days is condemned. Less than 10% of the urethra examined were found to tolerate a catheter of size 22 Ch. or larger for longer than a week and only this small group can be considered as suitable for this form of drainage.

(3) Urethrostomy drainage, though not ideal by any means, goes a long way towards solving many of the defects of the other methods. When bladder drainage is required pre-operatively urethrostomy has the great advantages of mechanical efficiency, simplicity and added safety over the other methods. As an alternative to immediate prostatectomy, particularly in the "poor-risk" case with extra-urinary complications, urethrostomy will, I

advised that there should be no delay in establishing urethrostomy drainage. Barney (1934) described the very simple method of performing urethrostomy with catheter and clamp which he had used for many years. Lewis (1943) advocated urethrostomy for drainage of the paralysed bladder and claimed that there was less leakage, less infection, better drainage, in fact many advantages over other methods.

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Section of Experimental Medicine and Therapeutics

President—Professor H. P. HIMSWORTH, M.D.

[June 8, 1948]

WALTER ERNEST DIXON MEMORIAL LECTURE

[Number 5]

Pharmacology and Biochemical Lesions

By R. A. PETERS, M.C., M.D., M.A., F.R.S.

It is a pleasant but nevertheless exacting task to be invited to the honour of delivering a W. E. Dixon Memorial lecture. It is many years ago since I sat at the feet of Dixon to learn pharmacology from him. Still a clear visual impression remains of the high collar, the cigarette and the pungent wit which helped so signally the discourse and practical class. One of my earliest remembrances of the Physiological Society is of a demonstration in the small Lecture Theatre at Cambridge in 1911, of Dixon and Halliburton. Later, I came to understand more the vivid research interest, which was the spring of his lively teaching, and, shortly after World War I, I had the opportunity of closer contact with him in research for the Government connected with Chemical Defence upon which we were both engaged, under the ægis of Sir Joseph Barcroft. He worked very hard (with S. E. Gooding) to discover clues to the action of mustard gas. This work like that of two continents of varied scientists during World War II brought no final answer—but it left facts of value. For instance, Dixon and Gooding observed that protein solutions and silk adsorb mustard gas, so that it does not lose activity by hydrolysis. This curious phenomenon is not yet properly understood. He stressed the fact that mustard gas forms no toxic breakdown products or toxic substances with cell constituents, an important fact in connexion with its action. He considered that the effect upon blood-vessels was a valuable clue and believed in the involvement of an axon reflex produced by the continuous irritation of sensory nerves by slow hydrolysis. The latter is not regarded as true to-day, but his freshness of mind and willing reception of ideas will always remain a vivid memory, as also his intensely experimental outlook. Discussion with him (as with Barcroft) led so often to a resort to the immediate experiment.

In Dixon's book on Pharmacology (1912) there occurs a remarkably modern account of cell biochemistry; he has written: "If we remove from a living cell all dead materials, water salts and ferments, is it necessary to assume that there is anything left? We think not and believe that there is no inherent difficulty in regarding protoplasm as a system of ferments co-ordinated together," and a little further on "Drugs . . . may have an affinity for any of the dead particles undergoing analytical or synthetic reactions, and thereby either stop or accelerate the cycle of changes, or they may produce their effect on ferments". This is a really modern outlook and yet further scrutiny of the book does not suggest that these enzyme conceptions were used. As I believe, this was because knowledge of the enzymes which mattered in the intermediary metabolism of the life of the cell and of their organization was not then available. What have the tremendous advances of the last twenty-five years in the enzyme biochemistry of the cell meant for pharmacology? It seems that pharmacologists have been reluctant to apply the new knowledge; even as late as 1942 there is little mention of the possible importance of biochemistry in pharmacology textbooks. In that most scholarly statement of A. J. Clark (1937) it is true that emphasis is laid upon the

believe, be found to yield far better results in the long run. Post-operatively it confers an increased margin of safety on complete closure after operations on the bladder or prostate. Furthermore drainage can be maintained indefinitely and so ensure sound healing of the abdominal wound in the most unfavourable conditions.

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[April 22, 1948]

The following cases and specimens were shown:

Hydronephrotic Twin Kidney.—Mr. CLIFFORD MORSON.

Pyelograms Showing Early Result of Rovsing's Operation.—Mr. JOHN EVERIDGE.

Two Cases of Double Kidney.—Mr. R. H. O. B. ROBINSON.

Kidney with Unusual Congenital Cysts.—Mr. B. H. PAGE and Dr. J. F. HEGGIE.

Pyonephrosis in Lower Half of a Double Right Kidney.—Mr. GEOFFREY PARKER.

Carcinoma of Ureter.—Mr. ALEX ROCHE.

(1) Large Diverticulum of the Bladder Removed by Operation. (2) Prostate and Seminal Vesicles Removed by Total Perineal Prostatectomy.—Mr. J. C. ANDERSON.

(1) Large Vesical Diverticulum Successfully Removed from an Octogenarian. (2) Orchido-vaso-vesiculectomy for Tuberculosis.—Mr. WILFRID ADAMS.

Foreign Body in the Bladder.—(1) Encysted Paraffin Wax; (2) Paraffin Wax (Mr. W. S. Mack's Case).—Mr. W. W. GALBRAITH.

Carcinoma of the Bladder.—Mr. F. R. KILPATRICK.

Carcinoma of the Bladder.—Mr. ASHTON MILLER.

Ectopia Vesicæ.—Mr. A. W. BADENOCH.

(1) Staphylococcal Inflammation of Urachus. (2) Congenital Pyonephrosis.—Mr. HENRY K. VERNON.

Heterotopic Bone Formation in Suprapubic Scar.—Mr. T. W. MIMPRISS.

Two Cases of Ureteric Transplantation for Systolic Bladder.—Mr. R. O. LEE.

Urethral, Prostatic and Vesical Calculi.—Mr. F. R. ST. G. STEAD (for Mr. G. NELIGAN).

Congenital Urethral Valve from Child of Two Years.—Mr. F. J. MILWARD.

initiated by attack upon enzymes. Indeed in retrospect it is curious to note how slowly the idea has been accepted that interference with enzymatic processes in intermediary metabolism in a tissue could produce abnormality, and that it was a fundamental method of approaching such a research.

VITAMIN B₁ AND CONVULSIONS

For many years now we have been interested in my laboratory in the detail of the biochemical action of substances causing pathological effects, and in particular in trying to understand the initial change. It is convenient to focus attention upon this initial biochemical step, by calling it a "biochemical lesion" (Gavrilescu and Peters [20]). I must first indicate how we came across the pyruvate oxidase system, an organized group of enzymes responsible for oxidizing pyruvate ($\text{CH}_3\text{CO COO}^-$)¹ which forms the main theme of my lecture. This was in the attempt to meet the challenge set by the opisthotonus signs induced in the rice fed pigeon by vitamin-B₁ deficiency because it seemed that something fundamental would be learnt when this was understood. After some search (with H. W. Kinnorsley [26]) a fault was found in the lactic acid metabolism of brain tissue. With the further discovery that this could be rectified *in vitro* by addition of the vitamin in parallel with the cure *in vivo* by dosing such birds with vitamin, and with the final delineation of the actively damaged stage as that involved in the oxidation of pyruvate, it became clear that the biochemical lesion was present in the intermediary metabolism of carbohydrate at the 3 carbon acid stage (Peters [35]). In 1939, some ten years after the initial discoveries, taking advantage of Lohmann and Schuster's proof that the co-enzyme for the decarboxylation of pyruvic acid in alcoholic fermentation was the pyrophosphate of vitamin B₁ (otherwise called cocarboxylase), Banga, Ochoa and myself [3] proved that the missing component in the brain system was this cocarboxylase. These experiments were done with finely divided brain tissue respiring in a suitable phosphate mixture with additions of pyruvate as substrate (fig. 3). At that time it was also shown that the enzyme system responsible for this oxidation of pyruvate was complex [4]; in fact that it consisted of a battery of enzymes, suggesting that the demolition of the pyruvate molecule required fire from several quarters. Fig. 4 shows that in the

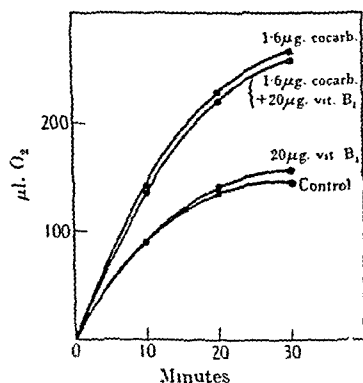


FIG. 3.

FIG. 3.—Comparison of the effects of vitamin B₁ and cocarboxylase on the oxidation of (0.018 M) in dispersions from avitaminous pigeon brain, in the presence of fumarate (0.004 M). (Data of Banga, Ochoa and Peters, 1939.) Reproduced by permission of the *Biochemical Journal*.

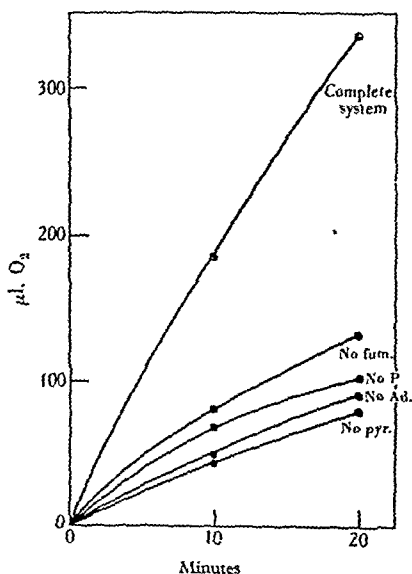


FIG. 4.

FIG. 4.—Effect of phosphate (0.05 M), fumarate (0.005 M) and adenylic acid (0.00014 M) on the oxidation of pyruvate (0.0091 M) by dialysed dispersions from pigeon's brain. 1.5 ml. enzyme (dialysed 2 hr.) to 2 ml. with additions including 0.1 mg. Mg.⁺⁺ (as MgCl_2). The complete system contains enzyme + Mg.⁺⁺ + phosphate (P) + fumarate (fum.) + adenylic acid (Ad.) + pyruvate (pyr.). Sample with no phosphate buffered with NaHCO_3 to pH 7.3. Air, 38°C.

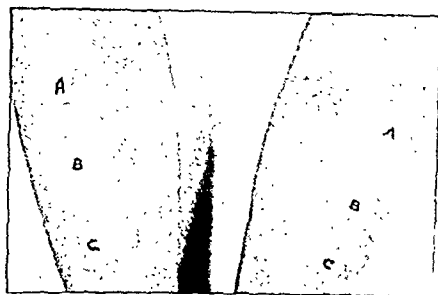
¹Throughout the term "pyruvate" is used rather than pyruvic acid; at the physiological pH the acid is mainly dissociated.

similarity observed in the poisoning of enzymes and drug effects in cells, but evidently he felt unable to carry the speculation further. As a matter of fact, pharmacologists have been right in their hesitation to lay much weight on the relation between drug actions and single enzymes; an exception is that of choline esterase and acetylcholine which formed the subject of the notable first lecture in this series by H. H. Dale [11].

I will try to relate pharmacology and toxicology with cell enzymes from the standpoint of biochemical lesions and modern biochemical research, in the hope of contributing to the further systematization of pharmacology. Though it is a commonplace that all pharmacological action requires as a first step contact and even some penetration into the tissue, it happens that recent advances in biochemistry have done more to clarify the enzymic constitution of the cell than to give us a clear picture of its varied mosaic surface. It seems more fruitful at this stage therefore to consider the enzymes. More especially the main emphasis will be upon collecting together threads of knowledge about the action of some toxic substances upon the enzymes known as the pyruvate oxidase system and of evaluating this in relation to some pharmacological problems. To do this, I shall speak in turn of some aspects of our vitamin B₁ work, of our work on arsenicals, and of some more recent investigations upon the poison fluoroacetate.

Let me first make the matter concrete by showing you the effects upon skin of the arsenical war gas lewisite, and of its antidote known as British anti-lewisite. Lewisite ($\text{CH}_3\text{CH}_2\text{CH}_2\text{AsCl}_2$) is a trivalent arsenical compound, discovered in U.S.A. by Lee Lewis in World War I. It is very quickly toxic upon injection into animals or when applied to skin and produces blisters when placed upon the human skin which take some twenty-four hours to develop. This type of arsenical penetrates skin because it is soluble in lipoids, and is hydrolysed when it reaches the aqueous phase to the oxide, which is still toxic.

As can be seen from these two photographs, for which I am indebted to the Staff of the Experimental Station, Porton, the blisters develop slowly. At the end of two hours, when the first photograph was taken (fig. 1), some erythema appears at the site of application of a drop of lewisite and some swelling may appear. Each of the forearms shown had application at A, B, C of a similar drop of lewisite two hours before the photograph was taken. The spots marked C were treated after two minutes with the current anti-gas ointment and BAL respectively. They show no erythema. Spots B and A show an erythema. Spots B were kept as a control; spots A were treated respectively with "anti-gas" and with British anti-lewisite. When seen at twenty-four hours (fig. 2), good blisters had developed in spot B,



Right Left

FIG. 1.—2 hours, BAL applied at A on left arm.



Right Left

FIG. 2.—24 hours, left arm at A no blister.

Photographs at Experimental Station, Ministry of Supply. (Reproduced by permission of *British Medical Bulletin*.)

and in spot A treated with anti-gas. The spot treated with BAL, however, showed neither vesication, nor erythema. Hence there was actual reversal of pathological change.

I have begun my lecture by showing these photographs because they put the practical end of one problem which it is wished to discuss more theoretically here. New therapeutic discoveries have so often come rather accidentally, that it is worth while to point out that this antidote was discovered by a theoretical approach, if you will by academic research. I wish to show the background and indicate the trend of the work. At first sight it must seem to be almost impudent to advance the view that such a complicated pathological process as vesication may be initiated by damage to cell enzymes, but that is an object of this lecture. Though the door is wider open to-day, it is interesting to record that this method of investigating toxicity problems required vigorous defence nine years ago; there was wide scepticism then among our scientific colleagues that the train of events leading to vesication could be

attack upon the enzymes with vesication. At the same time I showed that glutathione would not reverse the effect. So it came about that when the war started, this idea of attack upon SH groups and the selective action upon the pyruvate oxidase system formed the spearhead of our attack¹ upon the problem of finding antidotes.

Quite early in the war, tests upon several enzymes then available confirmed the selective action of the arsenicals; for instance the pyruvate oxidase system in a brain brei was much more sensitive to trivalent arsenic than the succinate system; the same applied to the α -glycerophosphate and to the triosephosphate dehydrogenases. As an illustration in a brain brei, 0.017 millimol lewisite poisoned the pyruvate oxidation to the extent of 89%, whereas the succinate oxidation was only 5% inhibited [38]. Also upon poisoning animals with arsenite or with lewisite, there was an accumulation of pyruvate in blood, just as occurs in thiamine deficiency [51], suggesting interference with the disposal of pyruvate. Evidence

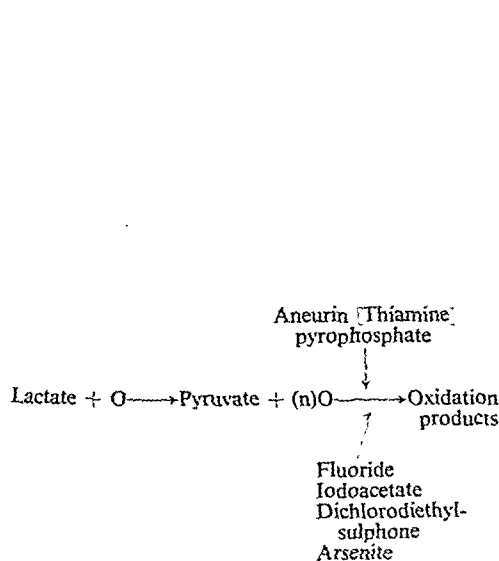


FIG. 5.—Course of oxidation of lactate by brain tissue and selective action of poisons. Cytochrome system not represented.

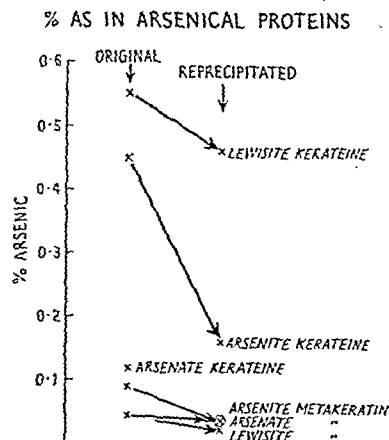


FIG. 6.—The diagram shows the original percentage of As in lewisite-kerateine, arsenite-kerateine, arsenate-kerateine, and in metakeratin compounds. The arrows indicate the change produced by a reprecipitation, which is slight for lewisite, though larger for arsenite. (From data of Stocken and Thompson, 1940.) In metakeratin sulphur is in oxidized (SS) form.

was also obtained (Thompson [50]) that lewisite interfered with the oxidation of pyruvate in skin, and that the enzyme system in brain contained an essential SH group [41]. This latter was dependent on indirect arguments used for other enzymes. From this it seemed clear that the pyruvate oxidase system could be used as an *in vitro* test, and in fact this proved to be completely justified.

At this stage it might be thought that the problem was virtually settled, and that the nature of the arsenical lesion was proved. If the arsenical attacked the SH group in the enzyme, there should be slight dissociation of the thioarsenite formed, and hence glutathione or some other such compound should protect, as was claimed to occur with arsenoxides and trypanosomes. Yet, in Oxford, it proved to be quite impossible to protect *in vivo* or *in vitro* from lewisite or arsenite with a variety of monothiol compounds (Sinclair). So we were faced with a dilemma and with no complete proof of the nature of the tissue arsenical compound. I will not go into the interesting story of how this matter came to be resolved, which depended at one stage upon an official discontinuance of the enzyme research owing to the prevailing scepticism. Suffice it to say that in connexion with a search for specific antibodies to possible lewisite-proteins, our colleagues Stocken and Thompson [45, 46] started to make and to analyse compounds of kerateine with these arsenicals; kerateine [22] is made by reducing the keratin in hair or wool. Upon adding these arsenicals to a solution of

¹The team who started work very early in the war consisted of two subgroups: upon the arsenical work H. M. Sinclair and R. H. S. Thompson; upon the mustard gas work E. R. Holiday, A. G. Ogston, J. St. L. Philpot, L. A. Stocken and R. W. Wakelin. After 9/10 months Sinclair and Philpot went to other work. Later, V. P. Whittaker and then G. Spray joined the arsenical work. Full discussions within the whole group took place at least once weekly. (For general review of BAL work see references Nos. 40, 55, 57).

absence of phosphate, of adenylic acid or of fumarate (in addition to the cocarboxylase), oxidation of the pyruvate molecule does not occur. I always find it exciting to realize that we might not any of us be thinking now unless this complex set of chemical changes were taking place in this simple 3 carbon molecule! A return will be made to a more detailed consideration of this enzyme system further in the lecture; it is very unstable *in vitro* in a ground brain preparation, being even damaged by freezing.

Turning to theory, it should be stressed that the opisthotonus signs clear up very quickly indeed upon giving vitamin, and that there is no detectable histological damage at this stage. It is in this sense an example of a pure biochemical lesion. This discourse has been started with a brief account of this ancient story because I regard the reversible change in vitamin-B₁ deficiency as the most definite instance in which it has been demonstrated that failure in an enzyme system, due to a lowered concentration of co-enzyme, can be related directly to the initiation of pathological change. As such it really illustrates the way in which biochemistry is at the basis of pathology, of pharmacology and even of medicine; for therapy will be most effective when the biochemical lesion is understood and reversed before it has gone too far.

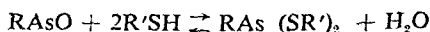
THE ARSENICAL LESION AND BRITISH ANTI-LEWISITE

Up to the present point, nothing has been said which would connect the action of toxic substances with the vitamin enzyme system mentioned. The most striking available example of this is the action of lewisite and of its antidote, to which I have referred already. War gas compounds like lewisite are not as a rule general protoplasmic precipitants. The investigation of this problem, which I initiated at the start of World War II for the Ministry of Supply, was based on two ideas as to the nature of the biochemical lesions induced, (1) that the trivalent arsenical compounds attacked SH groups and (2) that these SH groups were part of the pyruvate oxidase system. The reason for using these ideas can be considered briefly, as it bears upon the main problem.

SH groups and arsenic.—The idea that arsenic attacked SH groups was not new. Ehrlich suggested in 1909 that the arsenceptor might be either hydroxyl or sulphhydryl in nature. No experimental evidence was available until the 1920 decade, and this was inspired by Hopkins' researches upon glutathione.

These SH compounds give an immediate vivid purple reaction with nitro-prusside and ammonia; there are several varieties of sulphhydryl groups in living cells, differing in chemical reactivity. Hopkins delineated two important classes, small molecular substances like glutathione, and proteins containing the so-called fixed SH group, to be found with boiled muscle, skin slices and the like.

In work which is not well known E. Walker, working under my direction for the Government in 1923–25 [42, 54], found that diphenylchloroarsine as well as the vesicants mustard gas sulphone and allyl isothiocyanate attacked the SH group in skin slices and boiled muscle tissue. This we were inclined to connect with the toxic action, though mustard gas was an exception. Much better known is the more extensive work of Voegtlin and colleagues [52, 53] carried out about the same time, where they connected the actions of the therapeutic arsenicals, especially arsenoxide, with an attack upon SH groups of glutathione, getting partial protection against toxic effects by use of a large excess of monothiol substances. As Eagle [16] later confirmed, large amounts of the monothiols are needed to give protective effects. This is due to the dissociability of the thioarsinites, as shown by Cohen, King and Strangeways in 1931; in alkaline solution they readily break up according to the following equation:



These observations explain the use of the idea that As attacked SH groups, though at the very start of the work an N group could not be absolutely excluded.

ARSENIC AND ENZYMES

The idea that arsenicals might be attacking an enzyme was also an old view which Walker and I had discarded in 1925. The facts which led me to take it seriously again take us back to the pyruvate oxidase system. During the course of our vitamin-B₁ work, we had found that the poison iodoacetic acid had a selective effect upon the oxidation of lactic acid in normal brain tissue [37] similar to that of deficiency of vitamin B₁ in the avitaminous brain; both led to an accumulation of pyruvate. In 1935/36 I found that the vesicant mustard gas sulphone in small concentrations [36] had the same selective action and that minute amounts of arsenite behaved similarly; Krebs [27] had found previously that arsenite in high concentration inhibited oxidation of a ketoacids. This meant that the whole cytochrome oxidase system as well as the lactate dehydrogenase was comparatively unaffected (see fig. 5). Since iodoacetic acid was known to be a weak vesicant, and since Dierckx [12] and others had shown its combination with SH groups, it was natural that I should connect the selective

Before continuing with our recent work upon the nature of the enzymes, I wish to discuss further this important matter of reversibility and of dissociation, because it must ultimately shed light upon the exact nature of the groupings in the enzyme. The amounts of BAL required to reverse a combination of an arsenical may differ with change in the structure of the arsenical. With lewisite, very little excess of BAL suffices to remove the arsenic from the protein. But, if we take mapharside (arsenoxide), *in vitro* it takes more arsenic to poison the enzyme system suggesting that the compound formed is more dissociable; similarly more BAL must be used to reverse the combination [48]. This is confirmed by the behaviour of the compounds lewisite-BAL and mapharside-BAL which Stocken prepared. Lewisite-BAL gives no nitroprusside reaction on treatment with alkali, whereas mapharside-BAL gives a slight pink colour. If we turn to the toxicity a rather curious point appears. Lewisite-BAL has only about one-fifth of the toxicity of lewisite; this is also true for mapharside-BAL if excess of BAL is present; but in absence of added BAL, the mapharside-BAL kills animals (rats) quicker than the parent mapharside [39]. The explanation seems to be that the BAL compound being lipid soluble penetrates quickly to the active centres, where its dissociation enables the As to poison the cell. In fact with ciliates, we could not reduce the toxicity of mapharside-BAL by addition of BAL and I think therefore that there is some difference in the protein attacked. A rather similar phenomenon has been found at Porton by Harrison and Randoll [24] with tissue cultures. I am mentioning these points to indicate that although the main story is clear, there is still work required on the theoretical side, before we shall fully understand all the details involved in the action of arsenicals, and the influence of organic structure upon dissociability. It is worth mentioning also, in parenthesis, that an important practical application of the dissociability of mapharside-BAL is being made by Friedheim and colleagues [19] in New York. They find that these compounds readily kill some of the protozoa of disease (*T. equiperdum*), the BAL in this case acting as a carrier for the arsenic and is an antidote in reverse.

Fortunately any paradox raised by these theoretical toxicities does not matter in practical medicine where we have enough BAL present to act as chaperone. A lucky dividend for medicine came out of the search for the lewisite antidote both in the treatment of arsenical complications and of mercury poisoning. In the development of this, much help was received from workers in the United States; we have been using for treatment in this country an oily mixture of BAL in benzylbenzoate and arachis oil worked out by H. Eagle. The results given in Table I show the number of cases of arsenical dermatitis judged to have received

TABLE I.—TREATMENT OF ARSENICAL DERMATITIS WITH BAL

Response	Number of cases
Good	23
Fair	8
Doubtful	7
None	3
Patient died	3
	44

Mean time from first injection of BAL to complete (or nearly complete) healing was twenty-one days.

(British report, 1948 [7].)

benefit in a clinical trial organized by an informal conference of the Medical Research Council [33]. Similar results have been found in the U.S. [17].

This practical application in clinical medicine of a theoretical research serves to emphasize the possible benefits which can come from an academic approach.

To summarize up to this point, it seems to be reasonably proved that, speaking broadly, trivalent arsenicals combine with SH groups in the pyruvate oxidase system to form a ring compound; in any case it must be some enzyme which can be only reactivated with a dithiol compound.¹ Hence we have unearthed an enzyme system which can be inhibited both negatively by lack of a co-enzyme or positively by an arsenical. The biochemical lesion so caused can be sufficiently severe to upset the functioning of the tissue cells and initiate a pathological state like vesication. The particular part of the body which is poisoned will depend of course upon the distribution of the toxic or deficiency agent. Accordingly the problem of chemotherapy by arsenic may be redefined as that of attacking the pyruvate oxidase system in the micro-organism without poisoning this in the host. The degradation of pyruvate is a stage in intermediary metabolism which is particularly sensitive to pharmacological disturbance; there are strong grounds for the belief that it is reversibly inhibited in

¹When a greater concentration of the arsenical is present, more enzymes may also be involved even those capable of being reactivated by monothiois.

kerateine at physiological pH, the powerful SH reaction given initially is practically abolished; the amount of arsenic taken up was limited and definite for a given sample and not increased even on adding a large excess (see fig. 6). The uptake of arsenic was enormously reduced if the SH group was converted to SS by oxidation. The lewisite-kerateine compound was surprisingly stable, both to dialysis and to reprecipitation. The next point made was the crucial observation. When the number of SH groups disappearing was compared with the amount of arsenic combining, the surprising fact emerged that more SH groups were disappearing than atoms of As combined. From this followed the inference that the As was combining in a ring form (to the extent of some 75%). At once this resolved the dilemma, and showed how the arsenic might be at the same time combining with the SH groups in the enzyme, and yet be forming a more stable compound than the ordinary thioarsinites formed with monothiol, because a ring formation is usually considered to be more stable by organic chemists. The theory emerging which we call Stocken and Thompson's dithiol theory may now be given precise form in this figure (fig. 7), in which has also been included the 2:3-dimercaptopropanol, known as BAL; the idea is that lewisite formed with the protein in the enzyme a ring compound, of unknown ring size¹; the compound so formed though slightly dissociable is much more stable than any thioarsinite formed with a monothiol;

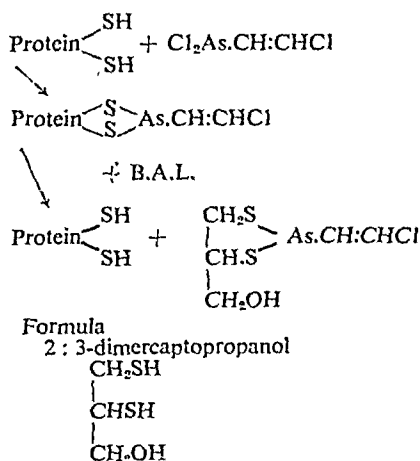


FIG. 7.

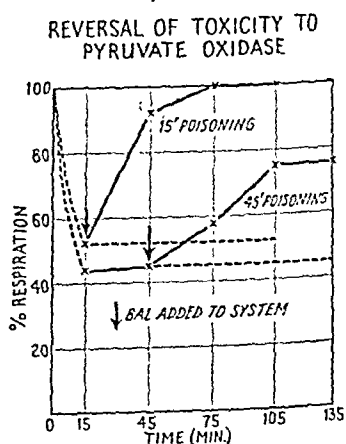


FIG. 8.

FIG. 7.—Dithiol theory.

FIG. 8.—Brain brei preparation (pigeon) poisoned by sufficient lewisite oxide to produce approximately 50% decrease in respiration. BAL added at the points indicated after fifteen to forty-five minutes of respiration. Substrate—pyruvate. (Data of Stocken and Thompson.) Reproduced by permission of the *British Medical Bulletin*.

hence any monothiol compounds formed will gradually transfer their arsenic to the ring. If any compound is placed in contact with the lewisite which forms a still more stable ring, there should be a steady transfer of the lewisite from the protein to the most stable state. BAL is such a compound forming a 5 ring; it was the third compound to be tried and was a new compound made by Stocken for this purpose. Oddly enough, it is still the least toxic of its class of skin penetrant dithiols, even though a large number of other dithiol compounds have been made here, in the U.S. and in Canada.

When tried on the pyruvate oxidase system, it was found that a series of dithiols including BAL would protect the enzyme against lewisite, when added at the same time, whereas monothioethyleneglycol (SH.CH₂.CH₂.OH) was quite ineffective. Fig. 8 shows an even more important point, that BAL will produce reversal *in vitro* of a 50% poisoning of the enzyme system when this is already established. Poisoning is complete in less than ten minutes with lewisite. Restoration with BAL is rather slow, suggesting that the respective stabilities of the ring compounds of protein and of BAL are not far removed in stability. If the interval is too long there is irreversible change. I have already shown the effects upon human skin; it has been also proved that the arsenic is removed from skin by treatment with the antidote and excreted in the urine [47].

This practical proof of antidote action *in vivo*, together with the theoretical background, removed any doubts about the nature of the grouping attacked in the enzyme system.

¹It has been deduced (Whittaker, 1947) that the stability of the ring formed with the enzyme-protein lies between "those of eight- and fourteen-membered thioarsinite rings".

vulnerable. If, as we believe now, it really is the pyruvate-tricarboxylic cycle, a large number of enzymes have to function in an orderly manner to fulfil this final stage in metabolism; the poisoning of any one part must damage the whole; since individual enzymes involved will have differing sensitivities to different poisons, compounds of widely differing constitution will produce the same biochemical result. A possible explanation is reached for one fact that puzzled us during the arsenic work; the total oxidase system was much more sensitive to the arsenicals than the pyruvate dehydrogenase component, which is responsible for the initial step. As both the pyruvate dehydrogenase and the α ketoglutarate dehydrogenase are sensitive to arsenic (and it may be other enzymes too), it would follow that the total system would be more easily poisoned. Pyruvate is not the only substance which is oxidized through the tricarboxylic cycle; the oxidation of fat is now believed to go this way after conversion to a 2 carbon fragment (Lehninger (29)).

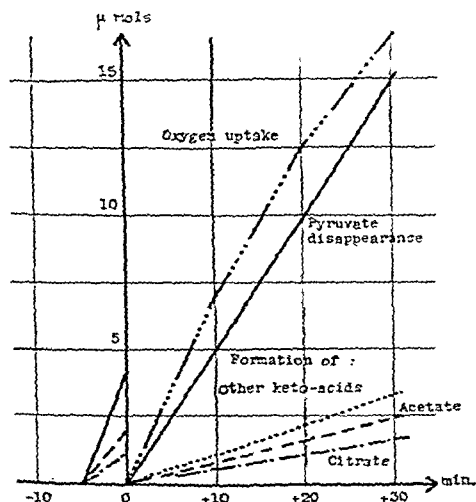


FIG. 10.—Dialysed brain dispersion (pigeon). The diagram shows in μ moles per respirometer bottle, the course of the oxygen uptake — ·····, pyruvate disappearance —, formation of citrate — (mainly α ketoglutarate), during a thirty-minute experiment with a dialysed brain dispersion (Banga *et al.*) at 38° C. In addition to pyruvate (0.013 M) fumarate (0.012 M), phosphate, Mg. ion, and adenine nucleotide were present. Appreciable amounts of citrate were formed in the preliminary period of incubation before readings of oxygen uptake were commenced. (Coxon, Liébecq and Peters—unpublished experiment.)

ACTION OF FLUOROACETATE

Following the theme which has run as a thread through this lecture, we should imagine that there will be other ways of producing a biochemical lesion in the tricarboxylic cycle, which would be equally damaging and equally able to initiate such processes as vesication. In this connexion, I will finish by mentioning the poison sodium fluoroacetate. The fluoroacetates came into prominence recently, and much work was done in England and in the U.S.A. Sodium fluoroacetate (as well as the acid) was first made in Ghent by the chemist Swarts (1896) and the sodium salt is now used as a rat poison. This table of toxicities (Table II) was compiled by Chenoweth and Gilman (1946) for methyl fluoroacetate. It is to

TABLE II.—TOXICITY OF METHYL FLUOROACETATE.
THE ROUTE OF ADMINISTRATION IS INTRAVENOUS UNLESS OTHERWISE SPECIFIED
LD₅₀ mg./kg. of methyl fluoroacetate

		Cardiac response	CNS response
Group I			
Rabbit	0.20-0.25	Ventricular-fibrillation	None
Goat	0.60	Ventricular-fibrillation	None
Horse	0.50-1.75 (i.m.)	Ventricular-fibrillation	None
Spider monkey..	14.0	Ventricular-fibrillation	None
Group II			
Cat	0.5	Slight	Marked
Pig	0.4 (i.p.)	Response of both heart and brain about equal	Marked
Rhesus monkey	4.0	Ventricular-fibrillation	Very slight
Group III			
Dog	0.06	None	Marked
Guinea-pig ..	0.35 (i.p.)	None	Marked
Group IV			
Rat	{ 5.0 (i.m., s.c.) 4.0 (per os)	Atypical	
Hamster.. ..	2.5-5.0 (i.p.)	Atypical	

narcosis (Quastel [43]), and that it is much involved in oxygen poisoning (Mann and Quastel [32]; Dickens [13]).

Further definition of the pyruvate oxidase system.—Let us now examine some possible reasons for this sensitivity, which lead to a more useful generalization. I have mentioned already one relevant point; the system in brain was proved nine years ago to consist of a battery of enzymes, fumarate being an essential catalyst. For some time there have been two possible biochemical explanations for the necessity of fumarate: (1) that of Szent-Györgyi that it had a special catalytic action in the H transfer, or (2) that it is essential for the oxidation of pyruvate by some cyclical process. The most modern and interesting form of such a cyclical process is that proposed by Krebs [28], which combines features of earlier schemes by Toennisen and Brinkman, Szent-Györgyi and Knoop and Martius into a unity known as the tricarboxylic acid cycle (fig. 9).

The essential feature of this scheme is that a 2 carbon fragment formed by oxidative decarboxylation of pyruvic acid condenses with a 4 C dicarboxylic acid formed from fumarate. So there is formed a 6 carbon acid *cis*-aconitic acid (containing three carboxylic groups in the citric acid series). By a successive series of transformations this becomes 5 carbon and 4 carbon and so the process starts again; in one round of the cycle there is degradation of one molecule of pyruvate to CO_2 and H_2O . This scheme is very attractive because it explains successfully not only the method of degradation, but also the biological reason for the presence in most tissues of such a strange group of enzymes in such high activity. Krebs and his colleagues have worked out the scheme for muscle, kidney and liver, and there has been much modern experimental evidence in its favour. For reasons which I

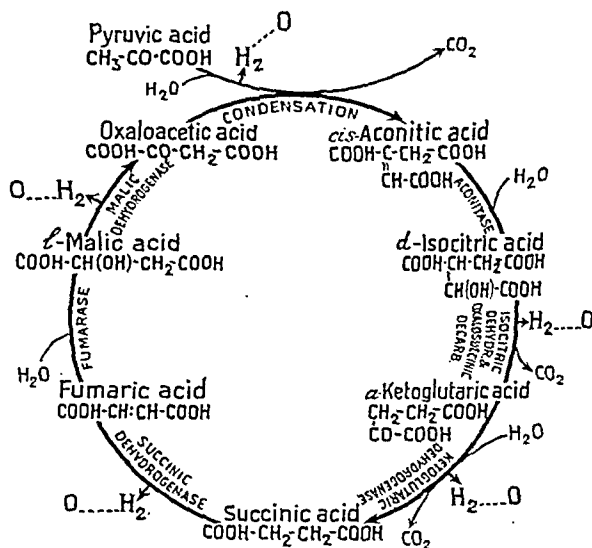


FIG. 9.—The diagram represents the reactions of the tricarboxylic acid cycle, in which a 2 C fragment formed from pyruvate is condensed with oxaloacetate to form a 6 C tricarboxylic acid (3 COOH groups). This is then degraded to acids with 4 carbon atoms. CO_2 is split off at various points of the cycle, and also H_2 , which is taken up by the cytochrome system. During one round of the cycle, one molecule of pyruvate is degraded to CO_2 and H_2O with uptake of 5 atoms of oxygen. (After T. Mann.)

cannot enter into here, until very recently we were not able to satisfy ourselves that it applied to brain tissue. However, during the last few weeks, Liébecq, Coxon and myself have succeeded in removing some of the major objections, which existed before, and now I feel no reason to doubt that the tricarboxylic cycle in some form applies to the brain preparations which we have used. In extension of our previous work [4] Long [30] had been able to show that in presence and absence of fumarate, the same amount of pyruvate disappeared; but that when fumarate was present the pyruvate was more completely oxidized. We have now found that when fumarate is present with the pyruvate, there is an accumulation of citric acid as well as of some α ketoglutarate. Citric acid is not directly on the path of the cycle, but is in equilibrium with the other 6 C acids (fig. 10). These facts are best explained by the Krebs idea that there must be condensation with oxaloacetate, and that the compound produced goes round the cycle. The acceptance of this view will mean some reinterpretation of the published facts; meanwhile we see at once why the pyruvate oxidase system is so

induce a metabolic block. This hypothesis is consistent with both the oxidation evidence of Saunders and with the competition theory of Guzman Barron.

If fluoroacetate enters the cycle, why does it not interfere with the tissue respiration *in vitro* of the pyruvate oxidase system in brain? This can be explained speculatively as due to the fact that our brain preparations are unable to oxidize either acetate or citrate; they lack therefore the factor which will bring fluoroacetate into play with the cycle, and already have a partial block at the citrate stage. *In vivo*, presumably these factors must be present, but again this must be a subject for further research.

As it is our general view that fluoroacetate has a poisoning effect upon the reactions in the tricarboxylic cycle, it would be expected to have vesicant effects; it is therefore interesting that Bacq, with Goffart and Angenot [1], classes fluoroacetic acid among the "vesicants".

The pyruvate oxidase system has turned out to be even more complex than was imagined in my original statement that it was a battery of enzymes; at the same time it is also more of a biological unity, and it is this which is susceptible to pharmacological attack. In seeking the connexions between enzyme biochemistry and pharmacology, we shall be well advised to look among the organized enzyme systems rather than to highly purified single enzymes. In the course of this discussion it is surprising how near we have come to the statements of W. E. Dixon which I quoted at the start of this lecture.

Though the search for these enzyme "biochemical lesions" is not yet far advanced, I hope that enough has been said to indicate that it is a fruitful field for medicine as well as for pharmacology. Clearly there must be many other ways in which the balance of these reactions might be upset and so initiate a diseased state. It is well known to workers in this field that short periods of anaerobiosis may prove extremely dangerous to the subsequent activity of the enzymes; for instance the pyruvate oxidase system loses activity quickly in the absence of oxygen. Any disturbance of circulation *in vivo* may be potentially dangerous, as oxygen supplies are cut off. The real miracle is that these closely dovetailed reactions do not more often fail.

Before concluding, there are some general remarks which should be made by way of appendix. In dealing with the poisoning of cell enzymes, I hope that I shall not be thought to be unaware of the dominating importance of permeability and of physicochemical effects in many pharmacological actions. In the case of the arsenicals, it has been suggested from Hawking's experiments [25] that the puzzling acquired tolerance of some protozoa is due to an altered permeability to the particular compound. I have focused attention here on pharmacological actions upon the oxidation of pyruvate and upon the association of this with the tricarboxylic cycle because this leads to one simple generalization. It is natural to wonder why no attention has been given to the possibility of blocking the earlier metabolic reactions by which sugar and glycogen are transformed into the 3 carbon intermediate. Surely the sudden elimination of the source of energy at its origin must be dangerous, especially in a tissue primarily using sugar. Such actions have been already studied by biochemists; Dixon and Needham [14] and colleagues found that most vesicants attack hexokinase, and upon this based a theory of vesicant action. Hexokinase is the factor concerned in the first activation of glucose. Though inapplicable to lewisite because hexokinase poisoning can be reversed with a monothiol, the theory is nevertheless of much interest; and this effect may contribute to the total vesicant action in many cases.¹

As we have seen, our early feeling that effects upon -SH groups were implicated in the action of war gas substances has now been made concrete for the trivalent arsenicals as well as for mustard gas sulphone; G. Barron (with Singer) has even gone so far as to suggest that arsenicals are the prime agents for the detection of sulphhydryl groups in enzymes. How far is this attack general? In the last years M. Dixon and colleagues concluded that lacrimators (such as ethylchloroacetate) were specific inhibitors of these groups in SH enzymes, and, as a result of independent researches in Belgium during the war, Bacq [2] has advanced the generalization that the "war toxics" are "substances thioloпрives", eliminating essential SH groups either by combination or by oxidation. A good example of the terrific pathological damage produced in this way is that of sodium tetrathionate (oxidized sodium thiosulphate); this rapidly induces a severe kidney nephritis, almost certainly due to oxidation of SH [21, 23]. The "thioloпрives" classification is certainly useful, even though it does not apply to mustard gas or to fluoroacetate. I think it might be extended; substances producing biochemical lesions in the "cycle" might be also called "cyclotoxic" substances.

Any conclusions reached in the present state of knowledge must be, in some sense, provisional and can be only regarded as stepping stones to further work. It has taken

¹Recently, it has been found that adrenochrome also inhibits this stage [34].

be noticed that there is a rather wide variation in toxicity to different animals, and that there are two types of action, nervous and cardiac. In the rabbit for instance the signs are mainly cardiac, leading to fibrillation; in the dog, on the other hand, the nervous signs predominate and doses as small as 50 $\mu\text{g.}/\text{kilo}$ kill the animals with violent convulsions after an interval of two hours or so in which little is noticed. In the rat, nervous signs appear in one to two hours; if the animal survives, it usually dies with intense weakness in some twenty-four hours.

This toxicity is very remarkable because it is such a simple molecule, and differs little from that of sodium acetate; Swarts showed that the -C.F. bond is very stable. The action is therefore not due to liberation of inorganic fluoride and is quite different from that of iodoacetate; there is no reaction with an SH group. The Cambridge teams (McCombie and Saunders [31], with that of Adrian) have worked out that the toxicity resides in the $\text{F.CH}_2\text{CO-}$ grouping. Following the lines of Knoop's oxidation theory for fats, in a series of straight chain compounds containing an increasing number of C atoms, Saunders [44] and colleagues have found that those with an even number of C atoms were toxic and those containing an odd number are not so. It seems to be inconceivable that this simple fluoro-compound can produce permeability changes and likely that it intervenes in an enzyme system. Initial attempts in 1943 by several of us in this country were unsuccessful in finding any enzyme inhibited by fluoroacetate; indeed (with Wakelin) I could find no effect at all upon the oxidation of pyruvate in brain tissue. There is not yet any known case in which fluoroacetate inhibits a single isolated enzyme. Guzman Barron and colleagues [6], however, took up the acetate analogy and found that in several more organized tissue preparations (slices), there was a competition with acetate; addition of fluoroacetate to the preparations led to accumulations of acetate. They therefore proposed that the compound was a competitor for acetate, and that it prevented oxidation of this via the tricarboxylic cycle. On the whole the amounts used by the U.S. workers to produce *in vitro* action were considerably larger than the doses giving *in vivo* toxicity. Liébecq and myself decided to use fluoroacetate some eight months ago in the hope of shedding light upon the nature of the 2 carbon fragment involved in pyruvate oxidation. We have found some interesting new facts, which I thought that you would like to hear. Most of our work has been done with a finely ground preparation of guinea-pig kidney, using a very pure sample of sodium fluoroacetate, kindly presented to us by Dr. B. C. Saunders. We soon found that the poison is involved in enzyme reactions in the tricarboxylic cycle other than those of acetate. Unlike brain, our kidney preparations oxidize fumarate well and pyruvate badly. Fluoroacetate inhibits fumarate oxidation with accumulation of citrate (Table III); citric acid is normally well oxidized. Hence fluoro-

TABLE III
Kidney homogenate
(Guinea-pig) (0-120')

Substrate	$\text{O}_2\mu\text{l}$	Acetic acid	Citric acid
Nil	0	—	—
Fumarate	462	0.1	0.18
Fumarate + Fl.Ac. ..	275 (-40%)	0.1	0.365
Pyr. fum.	545	0.05	0.60
Pyr. fum. + Fl.Ac. ..	461 (-15%)	0.15	1.00

(Fl.acetate 0.0033M)

(Liébecq and Peters—unpublished.)

Table III shows per respirometer bottle the uptake of oxygen in μl and the formation of acetic acid and citric acids (mg.) by a guinea-pig kidney homogenate in two hours at 38°C., and suitable phosphate medium containing the substrates mentioned. The differences in the amounts of acetic acid are not significant owing to the experimental error. Addition of fluoroacetate causes increased accumulation of citrate.

acetate also intervenes in the actual reactions of the cycle. Furthermore under appropriate circumstances, we have found a toxic effect *in vitro* with amounts of the order of those acting *in vivo*.

This has led us to a somewhat different conception of the action of this interesting inhibitor. In agreement with the findings of Barron and his colleagues, it will compete with acetate as a 2 carbon fragment entering the tri-cycle; but it has the further effect that it will block the cyclical reactions by intervening at some stage between citric acid and oxaloacetate; this we believe to be the more important action. One possible way in which the block may be produced is by actual synthesis of fluoro *cis*-aconitate, which we are now investigating. If further work substantiates this hypothesis, it will be a first example (perhaps) of the building in of such a fragment by intermediary metabolic reactions to

Section of Laryngology with Section of Otology

COMBINED SUMMER MEETING HELD IN BRISTOL

LARYNGOLOGICAL SESSION

[July 2, 1948]

Chairman—A. J. WRIGHT, F.R.C.S. (President of the Section of Laryngology)

Recent Progress in Nasal Physiology

By ARTHUR W. PROETZ, Saint Louis, U.S.A.

At first thought I had intended to pick up the thread where I had left it in a presentation before this Society in 1938 (*Proc. R. Soc. Med.*, 31, 1405) and to bring it up to date by reviewing the literature of the decade. It quickly appeared that such a report would be misleading since progress during this time has, in some phases, rested much more upon older investigations than upon current ones. A few titles of articles appearing since 1938 have been appended. From these it will be seen that research on nasal physiology is still restricted and, as usual, highly specialized.

Before our day, interest was sometimes concentrated upon special investigations such as Braune and Clasen's work on nasal air pressures (1876) and Zwaardemaker's practical treatise on the physiology of smell (1895), but all this seemed fairly remote from clinical rhinology and very little effort was made to bring it closer. Probably the germ from which sprang our present interest was an article written by an Englishman in 1924: "Methods of Estimating the Activity of the Ciliated Epithelium Within the Sinuses", by A. Lowndes Yates. It somehow fired the imagination of investigators in this country and in America and led to a recrudescence of interest in the whole subject of nasal physiology. Co-ordination followed and finally the more systematic application of physiological principles to a none too satisfactory therapy.

It has been reiterated in the textbooks, in a detached way, that the nose moistened and heated the air for the lungs and that it was coated with a ciliated columnar epithelium. In practice, however, physiological processes were treated as something academic, which could be disregarded when the problem was one of eradicating infection. Emphasis was laid upon the "vestigial" character of the nasal structures. Since their importance in maintaining nasal health was not understood it cannot be said that they were wilfully disregarded but the unsatisfactory results of radical extirpation finally forced us to examine them more closely.

To-day we have learned to conserve tissues and functions wherever possible.

Whenever this question of conservation is introduced someone invariably cites cases in which conservation would be folly. I also have such cases. However, these are the exception and we have found it practical to suit our procedures to the requirements and not invariably to go the limit on the mere basis of supposed thoroughness.

Among the trends of the past decade the appreciation of ciliary activity in the nose and especially in the accessory sinuses undoubtedly is first in importance. Cilia are primitive structures surviving anything which does not destroy epithelium. They are powerful in their effect and they behave in an orderly manner. They are our best allies in the prevention and removal of infection and they cannot be indiscriminately done away with if nasal health is to be maintained. The fact that in the average adult nose there are areas of altered mucosa without cilia—and this without producing untoward symptoms—may have led us to underestimate them. Patches of pseudo-squamous epithelium result where the air can strike directly and for this reason they are either dry or accessible to blowing. But in the meatuses about the ostia, and certainly in the sinuses where this is impossible, cilia persist and it is desirable to maintain the continuity of streaming from sinus to ostium, to meatus, to nasopharynx

many years to reach our present limited conceptions of the pyruvate oxidase system. For those who feel impatient at the slow rate of progress in research, I can quote the text which hangs in the Hall of our Laboratory, and which we owe to the suggestion of the late Archibald E. Garrod, who was himself so much interested in the genetically induced abnormalities of enzymes leading to inborn errors of metabolism:

"For at the first 'wisdom' will walk with him by crooked ways, and bring fear and dread upon him, and torment him with her discipline, until she may trust his soul, and try him by her laws. Then will she return the straight way unto him, and comfort him, and show him her secrets."

[*Ecclesiasticus*, IV, 17, 18.]

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Entering a sinus surgically by enlarging its ostium is comparable to these experiments. It results in a denuded strip of injured bone and the tissue which forms in Nature's attempt to close the opening resembles the experimental fibrous septum and not the normal ostium.

Drainage artificially maintained by displacement over a period of time is preferable to instrumentation of any kind, since it maintains the continuity of ciliary activity.

In 1943 Hilding made a significant contribution to the controversial subject of negative pressure in the sinuses and more especially of its origin [5]. He introduced a needle into each of the frontal sinuses of a dog through the skull and connected them through tubes with separate manometers. A quantity of mucus was injected through another needle into one sinus, the other being used as a control. As the mucus was forced out through the ostium by the cilia the pressure began to fall in the manometer of that side, the other remaining stationary. The experiment was then repeated after killing the dog, to rule out possible air absorption. The results were the same except that the negative pressure was slightly less than in the living animal. The published graphs show a drop of 44 mm. of water in fifteen minutes in the dead animal. This is a negative pressure comparable to that produced by a violent sniff (50 mm. Braune and Clasen).

Ciliary streaming within a sinus does not approach the ostium in a haphazard pattern but assumes a roughly vortical character, the direction of whorl being opposite on the two sides [6]. This is of interest in view of a similar observation regarding the trachea and bronchi by Barclay, Franklin and Macbeth (1937, *J. Physiol.*, 90, 347).

It has been observed that stimulation of the intact vagus in dogs causes a vigorous constriction in the nose with a drop in nasal air pressures without affecting the general circulation as evidenced by the femoral blood-pressure [8]. Injection of histamine into the circulation causes a dilatation of the nasal vessels, but the effect in this case is general although there seems to be a certain specificity for the nasal vessels. Sympathetic activity is said to predominate following exposure to cold.

The absorptive capacity of the nasal mucosa is variable [10]. Any increase in blood and lymph circulation whether produced by physical or pathological agents increases absorption. The ease with which absorbable drugs are taken up by the sinus mucosa after displacement depends upon the viscosity. The absorption is apparently somewhat selective.

Protracted exposure to toxins of infection stops the activity first of mucous and then of serous glands [1].

The subject of lysozyme in the nasal secretions still appears sporadically in the literature. It is reported [13] that the lysis of test bacteria by nasal mucus is inhibited by acid concentrations which may be present "in the usual pH swings". In acid media adsorption takes place but no lysis. Change to a neutral reaction completes the cycle, but the bacteria may already have been killed by the adsorption, without being dissolved. The same author states that lysozyme disappears on the first or second day of a cold, and that there is none to be found in a "running nose". Secretions from hay-fever sufferers showed a high lysozyme content.

Some controversy still exists regarding the normal pH of the nasal mucosa. It seems likely that the figure closely approximates 7 under varying conditions and that the disparity in findings of various investigators is due to technical errors and the shifting reactions of the secretions on the surface [16, 17].

It has been shown clinically that deficiency of the thyroid hormone may result in changes in the nasal mucosa which can be recognized [25]. These changes may be either exfoliative in nature or resemble the pale, boggy manifestations of allergy. Patients deficient in the thyroid hormone commonly have an increased tendency to nasal infection which can be corrected by the administration of thyroid extract alone. Similarly, allergic individuals are less apt to exhibit nasal symptoms under an adequate thyroid supply.

as well as may be. Wherever disease or surgery results in a strip of non-ciliated epithelium in the path of the streaming there is a stasis of the mucus and conditions favourable to bacterial growth are set up. This is not always apparent on inspection for the normal mucus blanket is of microscopic thinness. The mucus is of such nature and of such minute quantity that unless it is augmented by exudates and the degenerative products of inflammation it cannot be seen. With a microscope and by other special means it can be demonstrated and in proportion to the size of the bacterial elements picked up it is completely adequate.

We were taught a generation ago, and with seeming logic, that removing a middle turbinate did not reduce the moistening surface of the nose so very much and that it could be sacrificed in the interests of drainage with relative impunity. To a great extent this is true owing to a circumstance not considered at the time, namely, that the middle turbinates are streamlined to the passing air currents. Thus, although the moistening surface is reduced, there is little interference with the distribution of inspired air. Minor changes of another type may be followed by distressing consequences. This occurs when the air stream is so obstructed or deviated as to project it in a concentrated jet against some restricted area or to deflect it away from some part of the nose, leaving an area unventilated.

As long ago as 1830 Bell described the constriction which exists approximately one centimetre proximal to the naris. Only recently was it pointed out that this constriction projected the initial air stream vertically, setting the pattern for its even distribution through the nose and being largely responsible for the prevention of local dry spots. Thus our predecessors, regarding the removal of nasal tissue wholly from the standpoint of its moistening function alone, did not hesitate to remove it extensively. We think of it now as upsetting the even distribution of air with its attendant mucus stasis and nasal infection.

We know also that the total moisture reaching the lung is not too dependent upon the retention of the nasal structures. It has been shown that breathing through the mouth supplies practically the same humidity at the glottis as breathing through the nose, with the important difference that the mouth soon dries while the nasal mucosa continues to supply moisture. There is one mechanical circumstance, however, which is commonly overlooked, namely, that the air channels are not a tube at all and certainly not a chamber but a series of extremely narrow slits by which arrangement all the inspired air is brought into intimate contact with the nasal surfaces. If we alter this condition the mechanics of nasal respiration are greatly upset.

That the nose is a filter has been known as long as anyone has paid attention to such things. "The nares", writes Cicero, "which are always open on account of necessary functions have narrower entrances lest anything which might be injurious should enter them, and they always are supplied with a moisture not useless for arresting dust and many other things." We know that this takes place through sifting, through impingement and through adsorption. It is axiomatic that a filter must be rid of the residue which accumulates upon it if it is to continue to function. This the nose does very well by means of the cilia and their mucus blanket. So long as these remain intact, infection cannot occur, largely for the reason that at the normal rate of progress bacteria which fall on the surface are carried past any given cell in something less than 1/10th second, a time too short for incubation and penetration [12]. What the effect of viruses may be in disrupting this system is as yet not clear.

Nevertheless we are confronted with the fact that all infectious ailments of the nose stem somehow from a single source, namely, the failure of the filter to cleanse itself. That this cleansing mechanism should have first consideration in every plan of treatment and surgery is only an extension of the old principle of maintaining drainage.

It has been shown experimentally that removing strips of mucosa within the sinus is not always followed by complete regeneration and results sometimes in fibrous septa, their extent depending in a general way on the width of the strip removed.

Gösta Dohlman (Lund, Sweden) asked whether the experiments with soluble dye were made on the living animal or on the preparation. He had put fluorescent particles in the nose and had not been able to observe that these soluble particles dyed the mucous membrane. This could be seen under ultra-violet light. He used fluorescent solution, which was carried away with the mucous blanket. He had tried to observe the same thing with pollen in hay fever, but he had not been able to trace what happened to the pollen. He wondered whether Dr. Proetz, working on these lines, had thought of the mechanism of action of the pollen as comparable with a soluble dye or a virus. Or was there some activity in the pollen particles themselves? Was there something in the action of the pollen, working itself down to the cell, which was likely to cause the allergic reaction or could the activity be compared with that of a virus or infectious agent in a watery solution?

R. G. Macbeth referred to the spiral movement of particles in the trachea. What did Dr. Proetz think was the explanation of this movement? If the particles did not go up in a spiral a certain number of them would reach the carinae at every bifurcation in the bronchial tree and tend to stick or to fall back again; but, in a spiral movement, there was greater likelihood that they would dodge the carinae and so reach the pharynx.

F. A. Pickworth asked what was the proportion of surface to blood-stream and lymphatic infections of the nasal sinus membrane. Professor Proetz had confined his remarks to surface infection, and the literature was vague on this question, except that it was established that in the specific infectious fevers the sinus membrane is always involved.

A point of interest concerning the cilia was their collective force. Sir Leonard Hill had shown that small brass weights were propelled along an excised strip of mucosa by ciliary activity. In numerous cases of histological sections of pus or mucopus in situ in a nasal sinus taken at autopsies on mental hospital patients, the mass had formed a ball which evidently had been turned round many times, so that there were layers—as indicated by the polymorphonuclear leucocytes—sometimes amounting to twelve or more.

A. W. Proetz, in reply to several questions, said that regeneration of the mucosa did take place in the right milieu. It was necessary to keep the surface as free as possible from the infectious material which accumulated in the viscous secretions. He used the displacement method in order to get the required vasoconstriction in the cells. This, since the solutions were retained for twelve or fifteen hours, got rid of the irritating substances on the surface. The next thing was to get the surroundings as moist as possible, especially during the hours of sleep. It was arranged that the nose should be in as nearly a physiological condition as possible by maintaining normal moisture and heat and keeping it perfectly free. If sticky mucus were left on the surface its presence was always an irritation.

The other thing which he used was a simple solution which he had found very useful—4% alcohol and 4% glycerin in normal saline. It was found a few years ago that the membrane could tolerate about 18% alcohol, so one was within very comfortable limits in using 4%. What he wanted to do was to have something which would stimulate the flow of mucus and then promptly get itself out of the way so that it would not be a constant source of irritation. Therefore they started with 4% alcohol. It stung mildly and then evaporated and disappeared, and the glycerin left behind held the moisture. If the patient were laid down and his head placed back it was slightly painful; he should be allowed to sit up and the solution be put over his turbinates. The action of this solution is the opposite to that of ephedrine. It was used every four hours for two or three days, and the nose was then given a chance to take care of itself. The blood came from small vessels into the mucosa, and he did not see why that should not be the path of the bacteria as well. He illustrated how the converging streams of mucus came along and the appearance of the section layer on layer.

On the question of spirals, he thought the theory of the Archimedean screw would be all right if the column of air were always upright, but in fact it was horizontal during sleep for eight hours of the night, and, moreover, it varied in different positions, being sometimes more uphill than at others. The drainage of the sphenoid was not entirely uphill; some of it was and some of it was downhill. He had the feeling that this was a developmental matter. In the trachea, considering the adjustment of the whole thing, he imagined that it would be better if the fibres were spiral than if they were longitudinal. He did not know about the accumulation of mucus at the carinae.

Apparently a small amount of injury of the nasal mucosa did not appear to make much difference. Numbers of people had considerable areas in the nose which were devoid of cilia altogether, and they got along just as well as other people. If the mucosa was anything like normal the cilia around the edge of an inactive area could pull the stream along for quite a distance, so that the inactive area did not really signify. There were no cilia in the pre-turbinate area, and yet the cilia at the margin were strong enough to carry the whole mucus right across the surface. If therefore the ciliated area were destroyed here and there it did not seem to make much difference, though if the destruction was at an important spot, of course, there was trouble.

In reply to a question on air circulation in the nose and the nasopharynx, this was checked by taking a section of a specimen head, not too emaciated, and pinching it between two plates of glass, then passing a current of smoke-laden air through the nose and taking motion pictures. It was found that a

The use of the extract and the dosage are best determined by the patient's response, the basal metabolic rate is of secondary importance and at times misleading.

This finding is in line with what is known of the general tissue reactions to deficiencies in the thyroid hormone. The symptoms arising in the nose which respond to thyroid administration, namely, extravasation, changes in the nature of the surface fluids, permeability, malnutrition, swelling and œdema, could logically result from these reactions. Any of them would render the mucosa more susceptible to infection and possibly to antigens as well.

This by no means touches upon all the individual observations in nasal physiology during the last ten years but it epitomizes those which are apt to have an influence on our clinical management of nasal disease.

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mucosa and be identified in the lymph of the cervical pathway, which shares with lymph elsewhere the fundamental property of collecting extravascular protein and returning it to the blood. The significance of absorption from the nasal mucosa of particles up to the size of egg albumin, and even serum albumin (mol. wt. = c.70,000) need hardly be stressed. Though the actual amount of matter absorbed is not large, substances to which the organism has become hypersensitive can evoke a vigorous response in quite small quantities. Many of the allergic conditions of the nasal mucosa could no doubt be accounted for in some such manner. Bacterial antibodies are usually globulins with a molecular weight of about 180,000, and are too large to pass through the nasal mucosa. Toxins are a good deal smaller, and since a slight amount of toxin can stimulate considerable antibody formation, the introduction of toxin (e.g. diphtheria) into the nose has been used as a means of securing immunity.

Particulate matter such as India ink does not traverse the mucous membrane after nasal instillation, nor do viruses, in a susceptible animal, pass through the nasal mucosa immediately. However, after a period in which they proliferate locally and become established in the mucous membrane, they then enter the cervical pathway and reach the blood in a steady and continuous stream. Working with rabbits, Yoffey and Sullivan (1940, *J. exp. Med.*, 69, 133) showed that vaccinia virus was not merely not prevented from reaching the blood-stream by the filtering action of the cervical lymph node, but that on the contrary lymph nodes form a perfect mechanism for the dissemination of virus. The cytotropic virus particles enter the lymphocytes which are constantly leaving the node, and the lymphocytes thus act as virus carriers which protect the virus while in the blood-stream, and enable it to reach any part of the body.

What is the exact origin of the lymph in the cervical pathway? In part it arises in the usual manner, from the capillary filtrate of the submucous blood-vessels. But it also seems certain that some of the cervical lymph is derived from the cerebrospinal fluid, leaving the skull through the cribriform plate in association with the emerging bundles of the olfactory nerve. It has been generally accepted that if care is taken not to exceed the normal pressure of the cerebrospinal fluid, simple crystalloids injected into the cranial subarachnoid space readily pass through the cribriform plate and reach the nose, while particulate matter on the other hand does not. Statements about particulate matter are difficult to assess unless one knows the size of the particles, an item of information which has been conspicuous in the literature by its absence. Recently Field, Brierley and Yoffey (1948, unpublished), studying sections through the cribriform plate, after injecting into the cranial subarachnoid space at physiological pressures a suspension of India ink whose particles ranged in size from $0.5\ \mu$ to $1.5\ \mu$, found that the ink particles passed freely along the course of the olfactory nerve bundles, both around the bundles, and in their substance, to their termination in the olfactory mucous membrane. Here the sub-epineural spaces containing the ink ended in the immediate vicinity of the submucous lymph vessels. There must therefore normally be a steady flow of cerebrospinal fluid through the cribriform plate into the nasal lymphatics, and possibly also through the nasal mucous membrane to the nasal cavity.

This centripetal flow must be sufficiently vigorous to transport ink particles, but as yet we have no way of measuring it quantitatively. It is interesting to note that in the monkey there is usually a steady spontaneous flow of cervical lymph, whereas in the cat and dog such a flow is exceptional. The occurrence of this spontaneous flow in a microsmatic animal such as the monkey—and presumably man—is possibly due to the increased volume of the brain and cerebrospinal fluid.

If bacteria and viruses behaved as inert ink particles, no infection of the nose would be likely to reach the brain, against the current of cerebrospinal fluid. On the other hand bacteria or viruses which obtained access to the cerebrospinal fluid—e.g. in meningitis—would certainly reach the nasal mucous membrane and the cervical

vertical rush of air was an invariable result; the air then spread out in various forms of eddies. A point which worried him was that he was not sure that the eddies were not to be considered in relation to the distribution of air in the back of the nose. There was a certain fallacy attaching to a model viewed through a glass plate. The septum was not the equivalent of a straight glass plate. His anatomist and he were trying to work out some nasal reconstruction by means of plastic in such a way that they could get a true representation of the nose, but they had to admit that noses, like other parts of the anatomy, varied, and this was a long job, and he did not yet know the answer. Comparative anatomy could be studied to any extent. The functions of the sinuses, for example, differed very greatly. In some lower animals, such as the seal, there were no sinuses. He had an idea that the sinuses might be insulatory in their nature. The giraffe, for instance, had a brain about as big as one's fist, and all the rest was sinuses—an air jacket.

He had no particular experience of the phase of the subject which Dr. Dohlman had developed. He had wanted to make it clear that he was not so much concerned with the infection of the cells and whether they could be stained as he was to try to work out some means by which an invading mechanism could stay in contact with one cell surface long enough to infect. If the substance was soluble it could spread over enough of the surface as it moved along to affect the viscosity of the mucous blanket and so make it ineffective. A slight variation in the mucus content had a great effect on the viscosity. If a soluble substance could bring that viscosity down to a point where the mucous blanket could no longer be pulled over the surface, like a tablecloth over a table, an opening was afforded for infection. This was admittedly theoretical.

As to the nature of the ciliary movement, nobody knew why it took that particular pattern nor what caused it. He had tried ways of getting enough magnification of the cilia to see whether they had any structure that would give an indication as to what made them move. The cilia were difficult to study and to photograph; they were packed closely and were highly refractile. It was like taking a photograph of a plastic hair-brush while the bristles were moving at 10 or 15 cycles a second. Sodium light had been used, also polarization; the stroboscope and the high-speed flash had been employed, but no structure could be seen in the cilium. It was the deduction of Seo (1931, *Jap. J. med. Sc. Tr. III*, Biophys., 2, 47) that the movement was nervous. Various experiments had been made, but the result was hard to evaluate. It might be a chemical stimulation due to potassium secreted at the end of a nerve. The subject was an open one.

The Nasal Mucous Membrane in Relation to the Lymph Stream and Cerebrospinal Fluid

By J. M. YOFFEY

THE nose in mammals possesses a rich submucous lymphatic plexus, which drains finally into the deep cervical duct or jugular lymph trunk. The deep cervical duct descends alongside the internal jugular vein to enter the thoracic duct on the left side, and the right lymph duct on the right. The deep cervical duct passes in most mammals through one large lymph node, but in monkeys and man the single large node is replaced by several smaller ones, strung along the course of the duct to give a characteristic appearance. Submucous lymphatic plexus, collecting vessels, cervical lymph node or nodes, and deep cervical duct together constitute a single functional pathway for the flow of lymph, mainly from the nose, but to a lesser extent from the mouth, pharynx and deep structures of the neck. We have called this the deep cervical pathway.

The deep cervical pathway can be clearly demonstrated as a functioning unit by the nasal instillation of a vital dye, as shown by Yoffey and Drinker (1938, *J. Exp. Med.*, 68, 629). The dye passes through the intact mucous membrane, enters the submucous lymphatics, and passes through the lymph node or nodes and the cervical duct to reach the blood. On subsequent dissection the pathway stands out very sharply—almost diagrammatically—and is deeply coloured by the dye. The more functional aspect of the pathway can best be shown if the cervical duct is first cannulated, and clear lymph obtained, and then dye introduced into the nose. It is only a matter of minutes before dye begins to appear in the cannula in gradually increasing concentration.

Not only dyes, but also proteins of low molecular weight, such as egg albumin with a weight of about 34,000, can readily pass through the living and intact nasal

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OTOLOGICAL SESSION

[July 3, 1948]

Chairman—DONALD WATSON, F.R.C.S.

(President of the Section of Otology)

Menière's Disease

By A. J. WRIGHT, F.R.C.S.

SUMMARY

FROM the results of a clinical and statistical study of 350 cases of Menière's disease the following conclusions may be drawn. Acute disease or surgical operation, particularly dental extractions, seem sometimes to be related to the onset of the complaint. Allergy and true migraine do not frequently coexist. Allergy in general is not an important factor. Long duration of the complaint does not seem to be an adverse factor in prognosis but advanced age does. The surgical treatment of infection in nose, mouth or throat does as a whole improve the prognosis as compared with cases not so treated.

Of such surgical treatment dental extractions are found to produce the most favourable results with tonsillectomy a good second; operations on the nasal sinuses, however, do not seem to improve the prognosis but this may be accounted for by their failure adequately to influence the relevant infection.

DURING the period of fifteen years or so in which I have been interested in Menière's disease I have accumulated clinical records and carried out a follow-up of some 350 private cases.

pathway; and while viruses would find no difficulty in traversing this pathway, for the reasons already noted, bacteria would be held up in the uppermost node or two of the chain. But since bacteria and viruses are not merely inert particles, but can spread by active growth, new possibilities of extension are thereby created as in the possible neurotropic spread of a virus such as that of poliomyelitis.

A. W. Proetz said that it had been noticed clinically in certain patients that they had an irritative process beginning in the nasopharynx and going downwards, so that within thirty-six hours the patient was left without a voice. Was there any evidence from any of these specimens that materials could pass down immediately below the surface in the lymphatics? Clinically there was evidence that it did. It was such a continuous process that one could almost predict when it would reach the larynx and then the trachea.

F. A. Pickworth had done experiments with human material on cerebrospinal fluid pathways using the ferrocyanide technique, and had published a figure (*Z. ges. Neurol. Psychiat.*, 1932, 141, 425) where the dye had passed along the maxillary nerve and had formed a collection in the antrum which contained pus, had a thickened membrane, and local hæmorrhages. The antrum of the other side was normal and the nerve showed no passage of the dye. Professor Yoffey had illustrated the passage of sizable particles along the cerebrospinal pathways to the nasal mucosa in a rabbit suffering from "snuffles"; had he any other evidence of increased cerebrospinal flow into the tissues in diseased conditions affecting the nerve sheaths?

J. M. Yoffey, in reply to several speakers, said that he found difficulty in answering some of the clinical questions. Unless results were checked and rechecked on the experimental animal they could not make a dogmatic statement about pathways of lymphatic spread. In experiments on the main cervical pathway, outlined after nasal instillation of dye, communications with parapharyngeal and paratracheal lymphatics were not infrequently seen, but they were not so well-filled with dye as the main cervical pathway, along which lymph from the nose normally flowed most readily. However, if the main cervical pathway were to be obstructed, these collateral sources of lymph flow, which undoubtedly existed, extended right down to the lower end of the trachea, and could presumably account for some of the clinical observations on the paratracheal spread of infection. The classical method of interstitial injection of lymphatics in the dead animal merely showed injection material spreading in all directions from the site of injection, and gave no idea of the direction taken by lymph in the living functioning pathway.

With regard to the lymphatic vessels of the tonsils, he had nothing further to add to what he had already said, namely that in the experiments described peritonsillar lymph vessels were always evident, but not vessels arising directly from the tonsillar tissue. According to Aschoff's original classification of the lymphatic organs, the tonsils possessed efferent but not afferent lymphatics. If these efferent lymphatics existed in appreciable numbers, the larger peritonsillar lymphatics would represent the collecting vessels into which they drained.

With regard to Dr. Pickworth's question the ferrocyanide technique, unless employed with scrupulous care, was open to the objection that the solution may diffuse quite rapidly through the tissues, even through the substance of bones, and therefore may not be too reliable an indicator of normal fluid pathways. Nevertheless it was highly probable that the sheaths of the other cranial nerves possessed the same properties as those of the olfactory nerves though to a lesser extent. Schwalbe among the earlier workers reported the escape of India ink from the cranium along the nerves of the jugular foramen, and there seemed no reason why, under abnormal conditions, other cranial nerves besides would not also permit the perineural spread of crystalloid or particulate matter. The speaker had no direct evidence of increased cerebrospinal fluid flow into the tissues in diseased conditions affecting the nerve sheaths. However, it seemed highly probable that inflammatory conditions with a fair amount of fluid exudate would be very likely to facilitate this passage.

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Nov.—OTOL. AND LARYNG. 1.

This paper gives the results of an analysis of this material in certain particular directions which would seem likely to help in the solution of the problem of the causation of the disease.

The cases studied had been followed up for periods varying from one to ten years with an average of about three years. The investigation has been particularly designed towards arriving at an answer to certain defined questions which might be expected to provide some evidence as to ætiology.

(1) *The reason given by the patient for the onset of the complaint.*—In the very great majority of cases the patient is as mystified as the doctor as to why this distressing disease should have come upon him. Of the 350 cases dealt with in only 30 was any cause suggested. Of these 30, however, I was surprised to discover that in 15, i.e. no less than half, a recent extraction of teeth was blamed for the onset of the complaint.

Causes	Number of cases	Causes	Number of cases
Extraction of teeth	15	Influenza	3
Trauma: Blast of motor horn ..	1	Hysterectomy	1
Head injury	2	Removal of tonsils	1
Syringing ear	1	Severe epistaxis	1
Acute tonsillitis	1	Childbirth	1
Pneumonia	1	Childbirth with eclampsia ..	2

I feel that this curiously high occurrence of dental extraction as an alleged cause can hardly be regarded as coincidental.

(2) *The coexistence of allergic manifestations.*—In the present analysis only 20 cases (6%) gave history suggestive of allergy: Asthma, 3; nasal allergy, 10; skin lesions, 5; angioneurotic œdema, 2.

While I have no control figures as to the occurrence of allergy in the general population the figure of 6% would not seem to be high enough to suggest an ætiological factor of importance.

(3) *Migraine.*—Care is needed in dealing with case-histories since the vertiginous attacks of Menière's disease are quite frequently diagnosed as migraine both by the medical attendant and the patient. From the present series of 350 cases in only 8 (2%) was there a history of attacks of a classical migrainous type. In a number of others migraine was mentioned but on investigation it became obvious that the attacks so named had been, in fact, vertiginous and associated with a labyrinthine lesion.

The figure of 2% for the co-existence of migraine and Menière's disease in the same individual would not seem to me to suggest any close relationship between the two complaints.

(4) *The duration of the disease or age of the patient as factors in prognosis.*—Length of duration of the disease does not appear to be an adverse factor in prognosis. Thus, while the average duration of the complaint when first seen in the cases later shown as cured or improved was five to six years, in the group of those in which no improvement took place the relative figure was five years. It would seem, therefore, that the duration of the disease is not an important factor in prognosis.

Age of the patient.—Some support would seem to be given from an analysis of this material to the view that the age of the patient is an adverse factor. Thus of the cases aged 50 years or less 65% were shown as cured or improved while the comparative figure for those over 50 years of age was 45%.

(5) *The importance, or otherwise, of a focus of infection in the aetiology.*—In 1940¹ I presented to this Section a contribution on this question based on a series of cases in which surgical treatment had been carried out for the removal of such a focus from nose, mouth or throat. The results then given seemed to indicate that such treatment favourably influenced the course of the complaint. On the other hand, the period which had elapsed from the time of operation was relatively short and no control figures were then available.

In my present contribution cases have been followed up, in some cases for as long a period as ten years and in these have been included both those treated on the infective basis and those untreated, so that some comparative figures are available. Cases are grouped in accordance with the surgical treatment adopted and the results are recorded in regard to the symptom of vertigo. In the table "cured" means complete freedom from vertigo, and "improved" means an absence of attacks but with some remaining general unsteadiness.

RESULTS OF SURGICAL TREATMENT OF INFECTION

Form of treatment	Number	Average period of follow up	Cured	Improved	Unaltered	Worse	Cured or improved %
Tonsillectomy	32	3.50 yr.	20	1	8	3	66
Dental extraction	22	3.00 yr.	16	2	3	1	82
Nasal sinus operation	12	2.25 yr.	2	—	7	3	17
Combined operations (more than one of above)	16	3.00 yr.	9	4	2	1	81
Total	82	3.00 yr.	47	7	20	8	66
Untreated cases	30	3.00 yr.	2	4	17	7	20

It will be seen that of the 22 cases of dental extractions 16 were cured as far as vertigo is concerned. Of the 32 cases of tonsillectomy, 20 lost their vertigo, but of the 12 cases in which surgical treatment for nasal sinusitis was employed only 2 lost their vertigo. Thus removal of teeth produced the most favourable results, tonsillectomy came next, with nasal sinusitis little better than an also-ran. Figures for those cases in which more than one operative procedure was employed gave results which compared favourably with those of the nasal sinusitis group, but were not as good as the cases of dental extraction and tonsillectomy.

From consideration of the table it would appear that the disease in untreated cases with few exceptions tends to progress, thus of the 30 such cases in only 2 did the vertigo entirely clear up.

A comparison of all cases treated surgically to eradicate infection in mouth, nose or throat with untreated cases as a control shows a figure of 66% cured or improved in the treated group as compared with 20% in the untreated.

Mr. Terence Cawthorne said that while focal sepsis might possibly play a part in the causation of certain forms of vertigo he did not think that such cases were frequent. One of the aspects of Mr. Wright's paper that he would like to emphasize was the pathology of this condition. It was well known, thanks to the work of Cairns and Hallpike, that the disorder which they now called Menière's disease, and which used to be grouped under the umbrella-like term of "Menière's syndrome" or aural vertigo, had a definitely pathological basis. For this Lindsay and others had suggested the title "hydrops of the labyrinth", as being pathologically descriptive. But there were other forms of aural vertigo which were not infrequently confused with Meni re's disease. Since the original observations of Cairns and Hallpike there had been some twenty or more cases in which the temporal bones had been examined post mortem and the symptoms in all these cases were practically identical,

¹Wright, A. J. (1940) *Proc. R. Soc. Med.*, 33, 459.

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cerebrospinal fluid could be reduced 50% by severe dehydration, and it seemed rational to think that one could do the same with the endolymph. He had been interested in the matter since 1935, when he heard of Temple Fay's work on the treatment of epilepsy by dehydration, and since then he had used this method in all his Menière cases. It also seemed possible that tea was an ætiological factor, as so many patients admitted that they were heavy tea drinkers, and attacks decreased after giving it up. He thought that tea might be a stimulant to endolymph secretion.

The following also took part in the discussion: Mr. E. J. Gilroy Glass, Mr. W. H. Bradbeer, Mr. R. D. Owen, Mr. J. C. Hogg, Mr. H. V. Forster and Mr. E. D. D. Davis.

Mr. A. J. Wright, in reply, said that Mr. Cawthorne had rather supported the use of the term "hydrops of the labyrinth". He was hoping they would get the name "Menière's" attached to this group. The material in his paper was selected on the basis of cases which, Mr. Cawthorne would agree with him, they were in the habit of calling Menière's disease.

A form of injury which he had encountered on one occasion was in the case of a lady who went for a long drive in the winter with the car window open and within a few hours she presented a typical picture of Menière's disease.

Mr. Davis had questioned whether one could have Menière's disease in which there was deafness and afterwards a return to normal. Occasionally one did find such cases. Out of the whole bulk of hospital and private cases he could recall two or three in which there was a considerable defect in hearing and afterwards a complete return to normal, but this was very exceptional.

There was no reason why any lesion of the labyrinth should not produce a somewhat similar type of clinical picture. Mr. Bradbeer had suggested that these cases arose because the function of the labyrinth had worn out in elderly people. But the point which seemed to him to be against that was the fact that this complaint was quite common in young people.

Mr. Owen had asked about middle-ear disease. That was a question they had discussed before. His own view was that it would obviously seem quite likely that inflammatory diseases in the neighbourhood would make the labyrinth itself more likely to become diseased, but from such studies as he had been able to carry out it did not seem likely that middle-ear disease was a causative factor in these cases. He was interested in the suggestion that sometimes the extraction of the teeth would apparently start the disease. He regarded that as evidence in support of the infective hypothesis.

Dr. Dohlman had mentioned milk as causing allergy; he himself had come across one case in which if the man took pork he got vertiginous attacks.

He suggested as a possible hypothesis for the mechanical explanation of obstructive attacks, alterations in the consistency of the endolymph. One had only to think for a moment of the series of small chambers communicating by extremely narrow passages through which the circulation had to take place, to realize how this might arise.

Mr. Angell James had stressed the suggestion that fundamental interference with resorption was a big factor. Possibly the reason for the attacks was a sudden obstruction in a portion of the labyrinthine circulatory system.

Purulent Pachymeningitis

By Sir HUGH CAIRNS, K.B.E., F.R.C.S., and F. SCHILLER, M.D.

IN this paper we report four years' experience of penicillin in the treatment of purulent pachymeningitis. Formerly the condition was almost always fatal, even after the introduction of sulphonamides: since the advent of penicillin 7 of our 15 cases have recovered, and these results should be greatly bettered now that penicillin is freely available and we are beginning to understand the problems of treatment. We have seen 33 cases of this disease in the last twenty years.

It will be best to begin defining purulent pachymeningitis by describing a typical case from the days before penicillin.

namely deafness, tinnitus, and spasmodic bouts of vertigo lasting a relatively short time. These bouts might occur at isolated intervals or in groups. The deafness had always been of the internal ear variety, and together with toxic deafness following quinine it was the only internal ear deafness which appeared to be reversible—a very important point he thought. Another thing about this deafness was the distortion of hearing which had accompanied it. The characteristic of the deafness in Menière's disease was a dislike of musical sounds or high-pitched sounds. The sufferers disliked music on the wireless, they disliked children's voices, and he had even heard them say that they disliked going to restaurants because of the clatter of knives and forks on plates producing high-pitched sounds. All the cases which he classified as Menière's disease, including two in which Hallpike and he had had the opportunity of examining the temporal bones, had exhibited these characteristics.

It was known that there were a large number of cases of so-called atypical Menière's disease—patients with postural dizziness or who had bouts of vertigo but no deafness, and others who had vertigo which lasted for a day or two and which was accentuated when they turned over in bed. There was this fairly large mixed group which in the past had been collected together under the term "Menière's syndrome", and although it was reasonably certain that the vestibular apparatus was at fault, it was not yet possible to say exactly where the fault lay. He did not think it fair to call them Menière's disease, because the pathological evidence was lacking.

The main difficulty in obtaining such evidence was that these attacks were never fatal and therefore the otologist never got the pathological material. He hoped that any otologist who had a fatal case of aural vertigo would ensure that the temporal bones and brain stem were made available for investigation. He was sure that the key to the better understanding of aural vertigo was more and still more pathological evidence of the underlying causes.

As to the ætiology of Menière's disease he agreed with Mr. Wright that patients with Menière's disease did not suffer more from allergy than did the ordinary run of patients. They had thought in the past that head injury played little or no part in the causation of Menière's disease—here he was talking of Menière's disease or hydrops of the labyrinth, and not of other forms of aural vertigo. But he could recall three cases of what he would describe as typical Menière's disease so far as the symptoms and physical signs were concerned which seemed to be precipitated by a head injury. This was a small number, much too small to permit any conclusion to be drawn and he was just mentioning them because he thought it was worth while making further enquiries into head injury as an ætiological factor.

He had had one interesting case of a patient who presented a typical picture of Menière's disease following an attack of mumps. The only atypical feature about this was that the patient had an almost complete deafness, but since the attack of mumps she had very typical attacks of giddiness lasting half an hour and going away, coming on again some days or weeks later. The similarity between that condition and hydrops of the labyrinth was so striking that he thought it worth mentioning.

On the question of assessing results, while naturally the vertigo was the important thing, he had found that the hearing was a delicate indicator of the state of affairs within the labyrinth. It was surprising how the hearing did fluctuate with the vertigo, and the hearing was something which could be measured much more easily than the vertigo. Admittedly one could do caloric tests, and the test results of vestibular function did vary, though not so quickly and delicately, he found, as the hearing, and he did think that in measuring the success or otherwise of conservative treatment the audiogram was an extraordinarily useful indicator. It had been to him a source of constant interest and, at first, surprise how the hearing in a case which by all tests was one of internal ear deafness, could vary as much as 40 decibels within a day. They had always thought that internal ear deafness was irreversible, but he knew hardly any other form of deafness which was so subject to variation as the internal ear deafness in Menière's disease.

Dr. Gösta Dohlman (Lund, Sweden) considered allergy an important factor and cited the case of a young man with severe attacks of vertigo which were abolished by elimination of milk from the diet.

Mr. J. Angell James said that if a group of cases of aural vertigo were taken they could be placed in two divisions, one in which there was undoubtedly a hydrops of the labyrinth, and the other in which the pathology was uncertain.

The hydrops may be accounted for in two ways, either there may be an increased secretion, or there may be failure of resorption of the endolymph. To his mind the failure of resorption seemed the more probable explanation, and on that possibility Cairns and Hallpike made an interesting point, that in their sections there was a definite fibrosis around the endolymph sac. This seemed an important possibility in preventing the resorption of the endolymph.

With regard to the control of the endolymph pressure it was well known that pressure of the

alterations of head posture, and penicillin does not pass freely between the blood and C.S.F.

In purulent leptomeningitis there are many cells in the C.S.F., and there are neck rigidity and the other signs of meningism. In purulent pachymeningitis there are few cells in the C.S.F. and little or no neck rigidity, unless and until the condition becomes complicated by leptomeningitis; the symptoms are those of a rapidly progressive paralysis of one or both cerebral hemispheres—hemiplegia, homonymous hemianopia, sensory loss in the paralysed limbs and, if the dominant hemisphere is involved, aphasia. Fits may occur in the early stages of this cortical paralysis. The temperature is usually higher than in leptomeningitis, probably because of the absorptive properties of the subdural space.

CAUSE

Purulent pachymeningitis is usually secondary to spreading osteomyelitis of the skull which is an unhappy sequel in some cases of pansinusitis. In our 33 cases the primary infection was in the paranasal sinuses in 23 cases, in the petrous bone in 6 cases, while in 4 cases the infection was from a distant focus. According to Turner and Reynolds (1931) the condition arises most commonly in chronic pansinusitis after some operative interference, sometimes no more than simple puncture of the maxillary sinus. As Dan McKenzie (1913) said: "What seems to be an irreproachable operation is followed by progressive osteomyelitis." The condition is clearly an uncommon one, but it has always made a deep impression because of the rapid intracranial spread of the infection and the almost uniformly fatal issue. One of the older otologists, describing the rapid spread of infection after some relatively simple and well-executed operation, said it was like setting fire to shavings.

ASSOCIATED LESIONS

We have described the pathology of this condition elsewhere (Schiller, Russell and Cairns, 1948) and it is only necessary here to mention the lesions which are associated with purulent pachymeningitis.

Spreading osteomyelitis of the skull was present in 26 of our 33 cases—in at least 26 cases for, as Dan McKenzie observed, the osteomyelitis may be overlooked. We have had a case in which at necropsy the skull vault was passed as normal by the pathologist, though at operation we had found beads of pus in the parietal diploe. Now that we have an effective antibiotic for this condition it is even more likely that spreading osteomyelitis will be overlooked unless the skull is repeatedly examined radiologically.

The osteomyelitis usually produces œdema and great venous engorgement of the overlying scalp; at operation the pericranium strips very easily and the exposed bone exudes blood from many points.

Thrombosis of the large dural sinuses or cerebral veins was present in 8 of our 33 cases, but Kubik and Adams (1943) found a higher incidence.

Multiple small cerebral infarcts have been found in some cases at necropsy. Loculated subdural abscess and cerebral abscess have become relatively common since we have been using penicillin and more will be said of these conditions later.

Leptomeningitis was a common sequel before the days of penicillin; also ventriculitis, when needling of the brain for abscess assisted the passage of infection into the ventricles. But these conditions have now become uncommon.

Lung abscess and purulent bronchopneumonia were seen in our series, and in this

This patient was a man of 47 seen by one of us with Mr. F. C. Capps in 1936. He had suffered from chronic pansinusitis for years and had recently developed an infected mucocoele of the frontal sinus with a lump on the forehead. Pressure on the lump produced a discharge of pus from the right nostril. Three months later both antra were drained of foul pus by the nasal route (*Str. hemolyticus* and in small numbers *Staph. aureus*), and drainage of the frontal sinuses was established by removing the anterior ends of the middle turbinate bones and external resection of the inner part of the floor of the right frontal sinus. For nine days the patient did well. Then he developed a spreading osteomyelitis of the facial bones with fever, swelling and abscess formation about the eyes and upper jaw, for which further operations were required. His wounds discharged much pus and he became weak, wasted and anæmic.

He was given sensitized streptococcal vaccine, prontosil and blood transfusions, but the facial osteomyelitis continued and, twelve weeks after its onset, spread to the frontal bone. During the next five weeks the osteomyelitis gradually extended backwards and the patient had headaches, facial pain and slight fever, and he became much more irritable.

Purulent pachymeningitis first showed itself on February 4, 1937, about sixteen weeks after the onset of facial osteomyelitis. The patient noticed a weakness and numbness of the right leg, and twelve hours later slight numbness and difficulty of control of the right hand; he vomited twice, had slight headache and fever (100.4°F.).

On examination there was slight hemiparesis and sensory loss in the right upper and lower limbs, more marked in the lower limb. Eighteen hours after the onset of these symptoms the patient began to show slight dysphasia, and right homonymous hemianopia. On the next day, February 5, he had gross aphasia, almost complete right hemiplegia, weakness and sensory disturbance of the left lower limb, incontinence of urine and fæces.

Operation on this day showed gross osteomyelitis of the skull, extending as far back as the parietal region, with subpericranial pus and extradural granulations. On opening the dura thick pus was found in the subdural space and small amounts could be collected for some time by depressing the brain away from the dura. Films of the pus showed streptococci and cultures yielded *Str. viridans*. The patient grew steadily worse and died on February 9.

In previous studies of intracranial spread of infection from the paranasal sinuses and mastoid little attention has been given to the subdural space. In their admirable work Logan Turner and Reynolds (1931) figure the dura as being in immediate contact with the arachnoid. In fact these membranes are separated from one another by a narrow space which usually contains a very small amount of fluid. This space may be occupied by a film of pus of variable thickness: the pus is not circumscribed in the first instance and may spread over part or whole of one or both cerebral hemispheres. This condition is called purulent pachymeningitis. If the condition is not cured at this stage, and the patient continues to survive, the pus becomes loculated by adhesions between dura and arachnoid to form one or more subdural abscesses. It is necessary at this stage to point out that not all subdural abscesses are secondary to purulent pachymeningitis; some, which are localized from the start, are secondary to necrosis of a patch of dura over the mastoid or frontal sinus, or are secondary to an abscess in the superficial part of the brain. We are not proposing to discuss these types of subdural abscess here.

In the early literature there was some confusion about the situation of subdural pus. Some cases of what was obviously purulent pachymeningitis were described as leptomeningitis. These two conditions, it must be emphasized, are quite distinct. The subdural space is quite distinct from the subarachnoid space; it is a single continuous space over the surface of the brain and spinal cord, except where it is crossed by blood-vessels and nerves, or where arachnoid granulations are embedded in the dura. Air passes readily from one end of the cranial subdural space to the other. Penicillin, as we have shown, passes readily to and fro between the blood-stream and any fluids which may accumulate in the subdural space.

The subarachnoid space, on the other hand, is a channel traversed by numerous fine septa and containing cerebrospinal fluid. Air in it cannot move freely with

alterations of head posture, and penicillin does not pass freely between the blood and C.S.F.

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connexion it must be noted that Williams (1944) of the Mayo Clinic has described a group of cases of pansinusitis accompanied by bronchiectasis. Some of our cases may have had suppurative lung lesions before they ever got subdural infection.

DIAGNOSIS

The multiplicity of intracranial infective lesions which are possible in any one case indicate the difficulties of diagnosis. However, the clinical picture of purulent pachymeningitis is sharply defined and although it bears some resemblance to uncomplicated cerebral thrombophlebitis it should usually be fairly easy to recognize. Cerebral thrombophlebitis as the sole cause of intracranial symptoms in cases of pansinusitis and spreading osteomyelitis must be very rare, if our experience is any guide. In cases of doubt there should be no hesitation in opening the dura to inspect the subdural space; and this can if necessary be done through an infected field—through an extradural abscess, for example—now that the infection can be controlled by penicillin.

BACTERIOLOGY

The predominant causal organisms of our series were streptococci of anaerobic, or viridans, or non-hæmolytic forms (Schiller, Russell and Cairns, 1948). Staphylococcus and B-hæmolytic streptococcus were rare: although the pus from the sinuses usually contained these organisms, the pus from the skull vault and from the subdural space usually contained streptococci of the non-B-hæmolytic groups. These organisms may be difficult to culture, and their bacteriological classification is still very ill-defined. They are for the most part sensitive to penicillin: all the cases which we have treated *adequately* with penicillin have given a good clinical response, and in 3 of 4 cases where the *in vitro* sensitivity was tested the organism was completely inhibited by 0.04 unit/c.c. penicillin or less. However, in one other case the organism was completely insensitive *in vitro* at the usual dilutions; there was some inhibition by 20 U/c.c. but none by 5 U/c.c. The *in vivo* sensitivity of the organism to penicillin could not be tested, owing to shortage of penicillin.

The occurrence of such relatively insensitive organisms indicates that in all these cases the sensitivity of the organism to antibiotics should be tested, and that until the results of the tests are available exceptionally large doses of penicillin should be given.

EXPERIENCE SINCE THE INTRODUCTION OF PENICILLIN

Since penicillin became available we have had 15 cases of purulent pachymeningitis. Five were incompletely treated owing to shortage of supplies, and, though the infection was modified, all died. Ten have been adequately treated and all but three have recovered.

The methods of treatment.—Systemic penicillin is given in doses of 100,000 units three-hourly, at least until the *in vitro* sensitivity of the organism has been tested. If the organism is normally sensitive the dose may be halved. As bone infection is notoriously prone to relapse, and as there is considerable risk of localized subdural abscess, systemic penicillin should be continued for at least eight weeks.

It is usually impossible to drain the subdural space. When we tried to do it in the old days the brain plugged the holes in the dura (intracranial pressure is often very high in this disease). We no longer attempt subdural drainage and instead pass one or more rubber catheters into the subdural space through burr-holes. Through each catheter large quantities of dilute penicillin are instilled at frequent intervals—6 c.c. of a solution containing 500 U/c.c., or as much as the subdural space will comfortably hold. Most of this solution is evidently absorbed from the subdural

space, for very little of it drains away through the catheter. The solution destroys bacteria, dilutes the pus, tends to prevent loculation and probably has the effect of producing a very high level of penicillin in the blood-vessels of the overlying skull, for some of the venous return from the subdural space passes through the skull bones.

We have not always succeeded in preventing loculation of the pus with formation of a subdural abscess, especially on the medial surface of the hemisphere, and at present we are not sure whether a catheter should be invariably passed along the medial surface of the hemisphere, and whether penicillin should also be instilled into the subdural space of an apparently healthy cerebral hemisphere. Further experience is required on these points. Our present belief is that the more the subdural space can be irrigated the less the risk of loculation.

Subarachnoid and ventricular penicillin is injected as required whenever leptomeningitis is considerable, or there is risk of ventricular contamination, and in the usual doses (10,000 to 15,000 units once or twice daily).

With systemic penicillin in full doses it seems unlikely that there will be need to remove large areas of skull on account of osteomyelitis. It should rarely be necessary to undertake massive removal of the skull vault in the acute stage, as used to be done. These mutilating and bloody operations are ill-supported by a patient who already has purulent pachymeningitis, and in our experience they rarely remove all the infected bone. In the later stages, however, it is important to remove any focus of sequestration and suppuration which remains, for, quite apart from the discomfort of discharging sinuses, these foci are apt to produce a recrudescence of intracranial infection once penicillin is stopped. It is well to note that osteomyelitis of the skull treated by penicillin produces novel radiological appearances and not every area of osteomyelitic rarefaction requires surgical removal.

VARIETIES OF RESPONSE TO TREATMENT

The methods described have been evolved gradually, and there is reason to hope that future cases will be more successfully treated than the present series. Only 2 of our 10 fully treated cases have run an uncomplicated course under treatment. The remainder have developed a loculated subdural abscess and two of them have also had an intracerebral abscess. Sample cases will now be described.

An uncomplicated case.—A soldier of 28 who had suffered for years from bad dental sepsis developed pansinusitis and bronchopneumonia. After a fortnight his antra were washed out and next day he developed acute spreading osteomyelitis of the skull and purulent pachymeningitis (*Str. viridans*). When he came under our care on the following day he had right hemiplegia and had lost all speech. He was treated with penicillin intramuscularly (2.5 MU) and subdurally (0.15 MU for fourteen days through a catheter) and also had a few subarachnoid injections. The neurological signs disappeared almost completely; the osteomyelitis of the skull also recovered completely with discharge of pus and spicules of bone from the site of one of the burr holes. During convalescence he developed signs of consolidation in his right lung but this also recovered. This patient was treated in April 1943. He was probably the first patient with this disease to be treated with penicillin. In the ensuing five years he has had several focal fits affecting the right limbs, but has been otherwise well and has been in regular work.

Purulent pachymeningitis followed by loculated subdural abscess.—A boy of 11 developed right maxillary sinusitis after toothache in April 1944. In July for the first time he became generally ill and a painful swelling appeared on the right side of his forehead. His maxillary antrum was washed out, and next day he became unconscious and showed right hemiplegia. He was observed to have focal motor attacks on the right side. Burr holes were made and pus was found in the subdural space in the left frontal region; cultures yielded anaerobic streptococci. He was treated with penicillin, as in the previous case, also with sulphadiazine, for at one stage early in the illness he had severe leptomeningitis as well. After preliminary improvement he deteriorated in the fourth week of treatment and a further operation showed a loculated subdural abscess on the medial surface of the left cerebral hemisphere. This was drained. The boy was desperately ill for nearly two weeks, then he made a slow and complete recovery.

Eight months later, as his nose was still discharging, Mr. G. H. Livingstone performed a Caldwell-Luc antrostomy and removed nasal polyp and the anterior part of the middle turbinate bones. Three years later the boy was well and had no residual signs apart from an incomplete right lower homonymous hemianopia.

The onset of loculated subdural abscess may be suspected in these cases when the hemiplegia fails to recover, or when after a slight degree of recovery there is retrogression. The lumbar puncture pressure also rises. The common site for the abscess is between the medial and inferior surfaces of the hemisphere on one side and the falx and tentorium on the other. The pus is found by needling through the intact brain and it can only be distinguished with certainty from an intracerebral abscess or pyocephalus by thorotrast pyography. The characteristic appearance is that the medial and inferior walls of the abscess shadow correspond to the falx and tentorium.

In 2 cases a subdural loculation was not recognized because its development had been masked by continuing penicillin treatment, and the patient subsequently developed a cerebral abscess. We consider it important to establish by means of ventriculography that patients with purulent pachymeningitis have no form of intracranial abscess before their penicillin is stopped and they are allowed to leave hospital.

General management.—These patients may be extremely ill for three to four weeks. Stupor may interfere with swallowing, so that the risk of aspirating fluids into the trachea and bronchi is considerable. For this reason we usually nurse our patients with the head low, by means of low blocks to the foot of the bed; they are usually fed for several days by indwelling stomach tube. Blood transfusions are valuable in the acute stage of the infection. A careful day-to-day clinical assessment and frequent examination of the pressure and cellular content of the lumbar C.S.F. are required in order to detect the onset of subdural loculation and other complications.

The primary focus.—Whenever a primary focus persists after the acute symptoms have subsided we believe that it should be dealt with radically. If possible this operative treatment should be deferred for some months and penicillin should be given systemically for a few days before and after operation.

Prophylaxis.—It seems likely that the incidence of purulent pachymeningitis, uncommon though it may be, could be further reduced with adequate prophylaxis with systemic penicillin, since a considerable proportion of the cases follow operations on the paranasal sinuses and petrous bones. Should penicillin be given before all such operations, or is it possible to foretell the cases in which such complications may arise?

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Mr. H. V. Forster desired to say a few words about prophylaxis. He would like members to tell if they had had experience of that rare complication osteomyelitis of the upper maxilla. It might follow quite conservative intranasal operations done to relieve chronic pansinusitis and which would include an intranasal antrostomy beneath the inferior turbinate.

He had seen very few examples of this complication, but the issue was fatal with eventual spread to the meninges, and in spite of post-operative treatment with the sulpha group of drugs in days before the discovery of penicillin. He could not account for the spread of this disease of the bone, except that one had sensed the poor general condition of the patient. One observed its slow advance upwards along the ascending nasal process and across the hard palate.

The surgeon would naturally dread the performance of extensive operations upon the bones of the face, though perhaps hope of recovery had rested with such drastic measures.

Ought we to use systemic penicillin treatment more often before and after operating intranasally on chronic cases of suppurative accessory sinus disease?

He had mentioned this complication in an earlier discussion at one of our meetings (December 5, 1947, see *J. Laryng.*, in press), and had had helpful replies from the opener and from members taking part.

Mr. A. M. Ross asked whether in operations when there was sinus infection the authors could specify whether it was the frontal or the maxillary or ethmoid sinus which was concerned. Was it one particular sinus or all the sinuses?

Mr. F. C. W. Capps said that he was unaware when he came to listen to this paper that the rather tragic case mentioned, and with which he had been intimately concerned, was going to form the basis of the discussion. That case was very fresh in his memory. It was a disastrous affair, and it was made the more disastrous in that the chronic sinusitis and the infected mucocele were found only in the course of a general examination of the upper respiratory tract. The man actually came for trouble in the external auditory meatus, and was persuaded that treatment was needed for the sinus disease.

He had had at least two other cases, one of which fairly recently had had a very happy sequel, thanks to the co-operation of a neurosurgical colleague, Mr. J. E. A. O'Connell. It was a relief to have now this penicillin regime, which could at least avert any trouble in a high proportion of cases. The question was whether in every simple intranasal operation on the antrum or ethmoid or other sinus they were to give prophylactic penicillin. It would seem at first sight an obvious thing to do, but penicillin had its disadvantages as well as its blessings. All those who had had experience of it would be prepared to say that it was a very unpleasant thing to have an allergic reaction in the case of a perhaps essential second course of penicillin after a very thorough first course had been given. Would Dr. Schiller consider it adequate if they waited for the first sign of something going wrong before attacking the case with prophylactic measures? In a high proportion of cases they would still have their penicillin in reserve and it might happen at a later date that it could be given without the unpleasant sequelae which sometimes attended a second course of penicillin.

Dr. Schiller had mentioned cases of thrombophlebitis as somewhat rare. He had certainly had two cases, both of which survived. The earlier was one in which he held his hand very considerably, as was now advised. It was the case of a girl who came in with an obvious orbital swelling, having had a sinus infection, and all that was done was to drain the peri-orbital tissues. She had a severe series of fits and the condition did rather suggest that it was not an ordinary case of meningitis. She recovered satisfactorily. This was before the days of sulphonamide or penicillin. At a later date he removed a deep sequestrum of the inner frontal crest from this patient. She had had a thrombophlebitis of the sinus with a spread of the phlebitis over the cortical area.

Another case was a child who was extremely ill with septicaemia and a hemiplegia. She had had a transient swelling over one eye. In that case he called in his neurological colleague, Dr. D. E. Denny-Brown, who thought it might be a thrombophlebitis and advised exploring widely the frontal area. This was done and a small, narrow, frontal sinus was found with a little bead of pus lying over the sinus. That child made an uninterrupted recovery. Thus of these two cases the one recovered as a result of masterly inactivity and the other as the result of extensive operation. It was to be hoped that these extensive removals in osteomyelitis cases were now at an end.

Mr. R. L. Flett said that he had seen osteomyelitis follow operation on the maxilla, but all the cases he had seen had been associated with polypi in the ethmoids or antra, with thick pus coming from the sinuses; and he thought that any case like that with cellulitis over the frontal bone should have injections of penicillin before surgery was undertaken. In this type of case penicillin was absolutely essential.

Mr. Norman Patterson said that he could recall only one case of osteomyelitis following operation on the frontal sinus, but he could remember three following operations on the antrum. One of these was a case on whom an operation on the other antrum had been done ten years previously without any complication. He was called in to see her because there was a slight swelling over the side of the nose. Large areas of bone were removed. In another case haemorrhage developed after intranasal antrostomy. The patient's nose was packed for about forty-eight hours; he soon afterwards developed osteomyelitis. The third case was one the late Mr. Herbert Tilley asked him to see. All three patients died. The other case following frontal sinus operation recovered after the removal of nearly the whole of the frontal bone.

Mr. E. D. D. Davis was of opinion that in cases where the possibility of osteomyelitis was expected a course of systemic penicillin should be given. If an extensive bone operation was to be done a course of penicillin should be undertaken before as well as after the operation. The earliest possible diagnosis of meningitis is of the greatest importance. Meningitis arising from the ear may be expected in certain cases. Children and young adults are more susceptible to meningitis particularly in cases of otitis media following scarlet fever and measles. The acute streptococcal mastoid of sudden and rapid onset in children was recognized by a profuse discharge of serous fluid from the ear, and when the mastoid was opened, the air cells were full of turbid serum: an osteomyelitis without localization.

Suppuration of the retrofacial mastoid air cells calls for a careful watch for threatened meningitis. A persistent headache with a slight rise of temperature and later vomiting is an indication of meningitis. An early diagnosis of meningitis cannot be made without an examination of the cerebrospinal fluid. Rigidity of the neck is a late sign and on two occasions he had seen a stiff neck resulting from acute adenitis of the glands of the neck. Both cases had been diagnosed as a meningo-encephalitis but they recovered in a few days. He examined the notes of 27 cases of meningitis with rigidity of the neck and only 4 recovered and these 4 were treated by large doses of penicillin and sulphadiazine. He believed the earlier the diagnosis and the more prompt treatment with penicillin and sulphadiazine the better the result.

The Chairman (Mr. Donald Watson), after saying how much the Section appreciated the paper, said that he had seen several cases of osteomyelitis in the frontal sinus cured practically without operation since the advent of penicillin. All the intervention that took place was the simple removal of pus. His own practice—he was thinking particularly of cases of polypi which had an underlying osteitis—was to use penicillin for twenty-four hours before operation and twenty-four hours afterwards. Thus one operated, so to speak, in a bath of penicillin and in that way infection was stayed. It was not necessary to give a long course of penicillin.

Dr. F. Schiller, in reply to the question as to whether it could be told which sinus was involved—the infection related to practically all the sinuses, and it was very difficult to single out one in particular. Certainly antral infection played a great part.

He wondered how important the problem of allergy and acquired resistance to penicillin really was, considering the life-saving properties of the drug.

Section of Proctology

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[May 19, 1948]

DISCUSSION ON RADICAL EXCISION OF CARCINOMA OF THE RECTUM WITH CONSERVATION OF THE SPHINCTERS

Professor G. Grey Turner: In my remarks I only wish to refer to two types of operation which I have practised, though very infrequently, during the last thirty-five years. These operations have unfortunately been designated "conservative", which is often interpreted as meaning restricted in extent of removal, although it was only meant to designate that the sphincteric apparatus is "conserved" and continuity of the bowel restored. In the one plan, intended for growths situated in the lower rectum, the operation is conducted from an extended perineal incision and would be better designated as "posterior cuff resection with preservation of the sphincteric mechanism". The other plan is an upper or anterior trans-abdominal resection with restoration of continuity and similar preservation of the sphincters. This method can only be employed for growths at the pelvirectal junction or in the first part of the rectum. Of course, there are many other types of operation with the same object in view and I profoundly regret that the most untimely and tragically sudden death of my friend, Professor Joseph Sebrechts of Bruges, robs us of the opportunity of hearing from his own lips of the technique and results of the type of operation of which he was such a master. I refer to the plan in which the most complete and careful mobilization of the growth from the abdomen was followed by the separation of the lowest part of the rectum and anal canal from below inside the sphincters, the mobilized bowel with the growth being then drawn down through the dilated anus. The operation was completed by the most careful suture of the divided colon to a fringe of anal mucous membrane preserved for that purpose. I saw Professor Sebrechts carry out this operation in September of 1931 and can give testimony to the sufficient extent of the removal and to the accuracy and painstaking work which was employed. On that occasion I was invited to examine a case in which the operation had been carried out three weeks previously and vividly recall that the sphincter grasped the finger very satisfactorily.

I feel that the only justification for my taking part in this discussion is because I can tell you of the long after-history of a very small series of the lower type of resection which I have closely followed for a quarter of a century.

NATURE OF OPERATION

Before entering into details I do want to say that the operation practised was radical in the comparatively small growths for which it was used in so far that the perirectal tissues with any embedded nodes were completely removed so that the inner surface of the levator was quite bared, the muscular fibres being plainly seen. The length of bowel removed in the posterior cuff resection is an average of about 10 cm. so that there is a sufficiency of free bowel above and below any growth that it is justifiable to deal with by this method. That I dared to try out this plan was because I was accustomed to see patients alive and well without recurrence some years after the comparatively limited perineal removal of those days and as time went on I got more encouragement from my own results. In retrospect I feel that I was justified—now that one can contemplate the really long-term results—as in the case of the patient still alive and well thirty-five years after an extended perineal removal with a sacral anus. In that case the growth was extensive and was adherent to the posterior vaginal wall which had to be partially removed. Another case which made a great impression I referred to in some detail in my Presidential Address to the sub-Section, as it then was, in 1926 (*Proc. R. Soc. Med.*, 1926, 19, Sub-Sect. Proctology, pp. 27-44). Part of the prostate and seminal vesicles had to be removed but the man survived in good health until his death from advancing years twenty-seven years afterwards. These and other similar experiences taught me the extreme importance and the rewards of thorough local removal. Actually my first resection with restoration of sphincteric control was done for what was said to be a gummatous condition which had resisted persistent efforts at cure by traditional means. I am able to show you a lantern slide of the specimen from which you can see that the upper division of the bowel was made well above the level of the bottom of the pouch of Douglas but the result, as regards function, was so entirely satisfactory as to prove a great encouragement.

LONG-TERM AFTER-RESULTS

In 1932 I related my experience of 17 cases of posterior resection with preservation of the sphincters (*Acta Chir. Scand.*, 72, 519) and my excuse for referring to that old material

Mr. E. D. D. Davis was of opinion that in cases where the possibility of osteomyelitis was expected a course of systemic penicillin should be given. If an extensive bone operation was to be done a course of penicillin should be undertaken before as well as after the operation. The earliest possible diagnosis of meningitis is of the greatest importance. Meningitis arising from the ear may be expected in certain cases. Children and young adults are more susceptible to meningitis particularly in cases of otitis media following scarlet fever and measles. The acute streptococcal mastoid of sudden and rapid onset in children was recognized by a profuse discharge of serous fluid from the ear, and when the mastoid was opened, the air cells were full of turbid serum: an osteomyelitis without localization.

Suppuration of the retrofacial mastoid air cells calls for a careful watch for threatened meningitis. A persistent headache with a slight rise of temperature and later vomiting is an indication of meningitis. An early diagnosis of meningitis cannot be made without an examination of the cerebrospinal fluid. Rigidity of the neck is a late sign and on two occasions he had seen a stiff neck resulting from acute adenitis of the glands of the neck. Both cases had been diagnosed as a meningo-encephalitis but they recovered in a few days. He examined the notes of 27 cases of meningitis with rigidity of the neck and only 4 recovered and these 4 were treated by large doses of penicillin and sulphadiazine. He believed the earlier the diagnosis and the more prompt treatment with penicillin and sulphadiazine the better the result.

The Chairman (Mr. Donald Watson), after saying how much the Section appreciated the paper, said that he had seen several cases of osteomyelitis in the frontal sinus cured practically without operation since the advent of penicillin. All the intervention that took place was the simple removal of pus. His own practice—he was thinking particularly of cases of polypi which had an underlying osteitis—was to use penicillin for twenty-four hours before operation and twenty-four hours afterwards. Thus one operated, so to speak, in a bath of penicillin and in that way infection was stayed. It was not necessary to give a long course of penicillin.

Dr. F. Schiller, in reply to the question as to whether it could be told which sinus was involved—the infection related to practically all the sinuses, and it was very difficult to single out one in particular. Certainly antral infection played a great part.

He wondered how important the problem of allergy and acquired resistance to penicillin really was, considering the life-saving properties of the drug.

returned. Now *twenty-two years* after the resection he remains perfectly well and the functional result has always been most satisfactory (fig. 2).

Professor Grey Turner then showed some slides of specimens exhibiting the main features of the growths when freshly removed. All came within the "A" group of Dr. Cuthbert Dukes' classification. The specimens were all columnar-celled carcinoma. In none of the examples was there obtrusive evidence of naked-eye involvement of the lymph nodes.

The speaker then continued: It is my experience of the outcome of this original series of cases which has established for me some faith in the method of resection with preservation of the sphincteric mechanism.

Of the few subsequent cases of posterior resection I only want to refer to the difficult case of a young man of 19 who was brought to me in London because a most competent

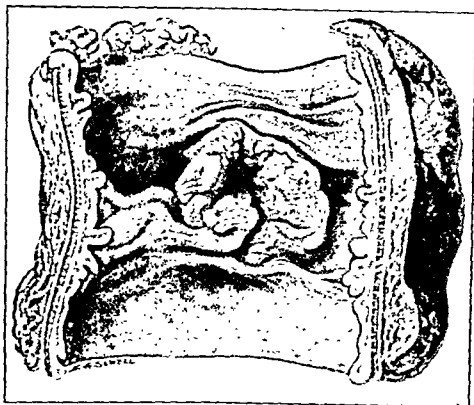


FIG. 2.—Patient alive and well 22 years after resection.

surgeon in the North had advised that a very small early lesion should be treated by so radical a removal that the patient at the outset of his career would be faced with a permanent colostomy. This young man when first seen was in excellent condition, his only symptom being constipation followed by diarrhoea and some local discomfort of two months' duration. On first examination "a mass was felt suggesting carcinoma" and on further investigation this proved to be a polypoid growth with a hard base on the anterior wall of the middle of the ampulla. This growth was removed for biopsy purposes and reported as so suspicious as to justify the surgeon in advising the very radical operation proposed. When the patient came before my notice six months later, all that could be detected was a hard indurated area the size of a finger-tip in the situation from which the material for the earlier biopsy had been removed. In taking what was considered a sufficiency for a further biopsy almost the whole of the nodule was removed. Histological examination disclosed the typical and unmistakable histological appearances of a columnar-celled carcinoma. By this time the assurance born of the knowledge of the long-term results in my earlier cases convinced me that a complete cuff resection with restoration would be justified and that was carried out, a portion of rectum about 12 cm. in length being removed. Healing was without infection and bowel function and sphincteric control were satisfactory. Now, seven years after the operation, the patient reports that he is perfectly well and without handicap from his bowel condition.

So that, in my hands, this lower or posterior resection has been encouragingly successful as the long-term records which I have presented exemplify. Incidentally, may I say that the method is valuable for dealing with the occasional example of large non-malignant papillomatous conditions in which the circumference of the bowel is involved (fig. 3). The well-known association of this condition with the development of malignant disease furnishes an adequate reason for the most radical treatment, and by no other plan can the base be really effectually removed while normal function is preserved.

TECHNIQUE

If the method is worth while, what of the technique? Thorough local anæsthetic infiltration may be sufficient to enable one to carry out the resection satisfactorily, but I feel sure it interferes with healing and especially in the presence of even mild infection. I have always employed general or combined anæsthesia as this leaves the surgeon free to discuss without embarrassment any difficulties that may arise during the operation.

is that I can give the full history of all those patients. Of the series 3 were simple and 14 malignant, one being a sarcoma. There was no mortality, no serious sepsis or other immediate complication and no permanent fistula or serious stricture. Of the 14 malignant cases 6 died with recurrence or dissemination within three years, and 1 died suddenly without recurrence two years and ten months after operation; the other 7 either died without recurrence or were alive and well more than five years after operation, all with satisfactory rectal function and control.

I am not proposing to make any apology for those who died with recurrence other than to emphasize that the cases occurred early in my experience and that in retrospect I now know that some were totally unfit for any but the most radical removal. In one case the patient had expressed the greatest horror of any interference which committed her to colostomy and as there was extensive glandular involvement it was considered that the conservative operation would give her as long a period of relief as any other method of excision and with greater comfort in the interval. As a matter of fact the local result was very satisfactory and colostomy was never required; the patient died of abdominal dissemination two years after the operation.

Let me concentrate on the group of those without recurrence; there were 7 cases and in all the functional result was satisfactory. In one of the earliest cases death took place from cardiovascular disease twenty-five years and two months after operation when the patient was in his 81st year. In this man we feared a recurrence eleven and a half years after the resection of the rectum but it turned out that he had developed a constricting carcinoma of the hepatic flexure. This was removed in one stage, bowel continuity being restored and thereafter his condition remained very satisfactory until his final breakdown only a few months before death occurred. In the next case the survival was for fifteen years, when death followed an operation for strangulated hernia. A diabetic in very poor condition at the time of the resection survived in comparative comfort for nine years when gangrene of a lower limb carried him off. Another was 74 at the time of the operation and convalescence was rather slow but she eventually did very well and lived alone in comfort in a distant part of the country, until death took place in her sleep eight years and four months after operation. Bronchitis, to which he had long been subject, carried off the next patient eight years after operation. Of the two surviving patients one, a female, is alive and well *twenty-six years* after the resection (fig. 1). A most competent surgeon had declared that only

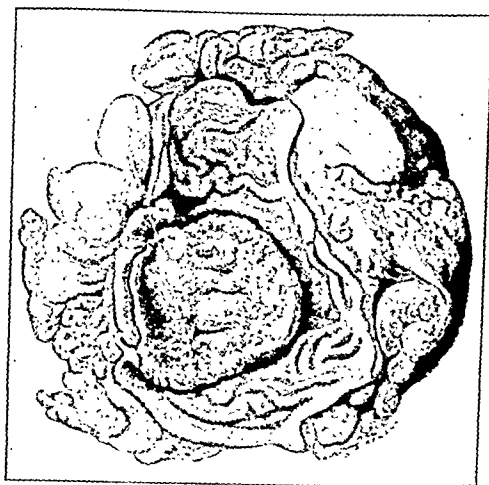


FIG. 1.—Patient alive and well 26 years after resection. (From *Acta Chir. Scand.*, 1932, 72, 530.)

a combined radical with a permanent colostomy held out any chance of success, but she knew much of the troubles of a relative who was the victim of colostomy and declared that she would rather die than submit.

The last of the group was a young man of 26 when he first came under my care. At such an early age I considered the prospects of cure after any type of operation, however radical, to be but poor and decided that he might as well have the benefit of continence till his disease

of the rectum must also be kept in mind. When the rectum has been dissected up as high as the conditions demand, it is divided and the upper end is then brought down and is laid in the sphincteric bed and is carefully stitched to the muscle and to the anal margin, the cut sphincter in turn being accurately repaired over the bowel. Though this operation is satisfactory it does not give such good functional results as in those cases in which the bowel can be transversely divided above the level of the sphincter and restored by suture. One difficulty is that the rectum, when brought down to the anus, occupies more space than the anal canal which it replaces, so that the suture of the sphincter is often rather under tension. Further it must be realized that the mucous membrane of the rectum is a poor substitute for the exquisitely sensitive lining of the anal canal.

There have been no serious complications and most of the patients have made quick recoveries, the average stay in hospital being just over six weeks, the shortest being three and the longest seventeen.

In nearly every case whether preliminary colostomy has been used or not there has been some infection of the wound, but it has always been slight and has remained localized and has never given rise to anxiety, and there has been no case of pelvic cellulitis. In most cases the temperature has never been raised during convalescence. In the past a more or less troublesome faecal fistula has been looked upon as the bugbear of this operation but in my series this complication has presented very little difficulty. In the one case in which there was considerable trouble in getting such a fistula to heal in a very fat lethargic man, a temporary colostomy had to be made to aid the process. This raises the question of whether or not colostomy should be carried out as a preliminary. I do not think it is essential, and question if the rectal wound has healed any better when it has been employed. Now I only make a colostomy where there happens to be some obstruction or the patient is in poor condition, and it is necessary to show what colostomy will do to improve it. In some cases I have first explored the abdomen to make sure that there has been no extension of the disease, but generally speaking I have not felt this step to be necessary in the type of case in which a conservative resection may properly be considered.

A complication which is often feared is stricture, but I have not found it to be a serious menace. In my first series of 17 cases there were only 4 examples and all were slight and easily controllable. In one case the condition was allowed to continue for five years because of the reluctance of the patient to have it attended to but at the end of this time it was easily cured by posterior linear proctotomy and the use of bougies.

The results from the point of view of functional capacity are what most concerns and interests both the patient and the surgeon. The most important point is the question of sphincteric control and this has usually been normal, and in all but one case at least entirely adequate. In the one case where the sphincter was incompetent the operation was done for a prolapsing sarcoma and the man had a patulous dilated anus at the time of the operation. As the disease rapidly recurred the sphincters never had a chance to recover their tone.

In operating for cancer the guiding principle must always be to remove the whole of the affected part with a wide area of healthy tissue, and the path of probable malignant invasion. Though this seems to be a too ambitious programme to be carried out by a comparatively limited excision there is probably a stage in all epithelial growths of the lower bowel in which this ought to be possible without the mutilating operations which are so usually required. The problem is to get the cases at an early stage and I have to admit that in my own experience it is only in about 2% of patients submitted to operation that I have considered the so-called conservative method justifiable. I must confess that at one time I was more hopeful about the prospects of this operation because I thought that a keener appreciation of the frequency of malignant disease of the rectum, an earlier resort to ordinary rectal examination by the practitioners who first see the patients and the more frequent use of the sigmoidoscope would probably result in many more cases being discovered at a stage at which this type of operation might properly be considered. To justify consideration of this method the growths should be small, not larger than about 3 cm. across, i.e. about the diameter of a two-shilling piece, and should be freely movable from side to side and should move up and down when the patient strains, and there must be no evidence of dissemination. Such growths will usually be discovered because hæmorrhage has been an early symptom or they will be found on routine examination and sometimes when unsuspected. They will usually belong to that type which is recognized as spreading on the mucous membrane and of the papillomatous variety (Dukes' Grade "A") rather than the infiltrating type in which the pararectal tissues and lymph nodes are early invaded.

For a time I expected that radium would be so successful in this type of case that operation would become obsolete but it is now recognized in Great Britain that in growths higher than the anal canal radium cannot be relied upon to bring about cure.

The case is so prepared that the rectum is as empty and as clean as possible. I prefer to operate with the patient in the left lateral position. An incision is made commencing at the side of the base of the coccyx and is continued forwards to the posterior margin of the anus. From just beyond the tip of the coccyx it follows the median sulcus. The posterior raphe of the levatores muscles is then divided in the middle line until the rectum is exposed inside its muscular bed. The rectum, with the whole of its surrounding pararectal tissues is then completely separated by blunt dissection until the inner surface of the levatores is left quite bare. This separation is carried out downwards as far as the upper border of the internal sphincter and upwards as far as the disease demands. In most cases this has meant opening the rectovesical or Douglas's pouch and dividing the bowel 5 or even 8 cm. above this point. After this section of rectum has been removed the ends are approximated and are carefully sutured end-to-end. The front of the anastomosis—i.e. the deep aspect in relation to the

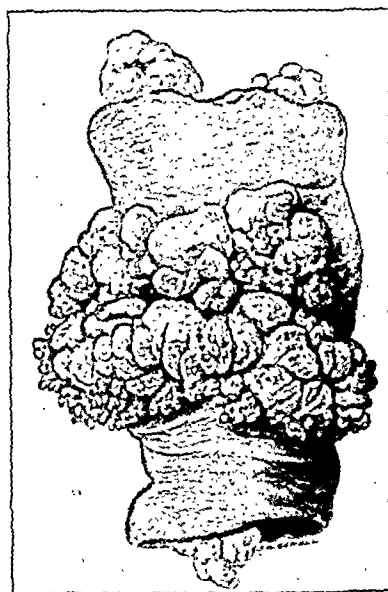


FIG. 3.—Cuff resection of rectum for encircling papilloma. The bowel is turned inside out. (From *Acta Chir. Scand.*, 1932, 72, 533.)

surgeon—is first approximated by a row of mattress sutures; by this means the cut edges are turned towards the lumen. A continuous, or once or twice interrupted, suture completes the union. In every case it has been possible to get the ends into apposition without tension, but this results in straightening the rectum so that it passes directly downwards from the pouch of Douglas or rectovesical pouch towards the anus instead of following the curve of the sacrum and coccyx. This straightening is very well illustrated in roentgen photographs made some years after the operation had been carried out. The suture of the anterior and lateral walls is usually easy and satisfactory and by the method described a certain amount of tissue is turned into the lumen so that when it heals it forms a ring-like shelf on the anterior and lateral walls. The posterior wall, on the other hand, cannot be tucked in to the same extent. After the anastomosis is completed the median raphe of the levatores is carefully drawn together by interrupted sutures. A small drain of soft rubber is placed inside the muscles, the other end being brought directly out of the wound. The skin and subcutaneous fat are securely sutured over the muscles. In order to avoid tension in the rectum from the accumulation of blood and mucus or flatus a rubber tube is passed through the anus and is left there for four or five days. In some cases the lesion may be so low in the rectum that the bowel cannot be divided above the sphincter without either encroaching on the growth or at least leaving an insufficient margin below it. In these circumstances I have carried the division of the raphe right through both the internal and external sphincters and have enucleated the mucous membrane of the anal canal under the guidance of the eye. This can be carried out very thoroughly, the only difficulty being caused by the forward pouching of the rectum which occurs anteriorly just above the internal sphincter and this must be carefully followed otherwise the bowel will be torn. The varying size of the ampullary part

mortality of this method has been higher than in the combined operations but the later results have been most encouraging both to surgeon and patient. So far I am not able to put before you the long-term after-results such as I have given for the perineal restorative operations but I am hopeful as to the future.

CONCLUSION

Coming from Newcastle-on-Tyne I feel that I may be expected to mention the Rutherford Morison plan of anastomosis, spoken of as "the intussusception method" with a long rubber tube. This operation has been rediscovered more than once and is sometimes spoken of as the Lockhart-Mummery method or after the name of Balfour. As a matter of fact, so far as I have been able to observe, this plan has not been very successful and it is significant that it has not been generally adopted. As an aid to anastomosis deep in the pelvis there may be a place for some mechanical device and I never forget that I am one of the diminishing band of witnesses to the great place which was occupied by the Murphy button in the development of intestinal surgery. In the days of my youth I invented an apparatus to facilitate this particular anastomosis. Though I have never actually used the apparatus (lantern slide) I think it might sometimes have an application and possibly some of the younger Fellows present may be disposed to ponder the matter and perhaps even to give it a trial, possibly with modification out of recognition.

I do not think that we must conclude that on matters of technique finality has been reached and on rather broader principles I have often thought that some combination of radio-therapy with radical surgery may turn out to be more successful than surgery alone. I say this remembering the remarkably suggestive results that were brought before this Section by Sir Charles Gordon-Watson now a good many years ago (*Proc. R. Soc. Med.*, 1935, 28, 1251).

It is, I consider, a worthy objective to aim at the preservation of the sphincteric apparatus but of course it must not be done unless it can be combined with a sufficiently radical removal. There are those who appear to be so satisfied with colostomy that they blind themselves to some of the unpleasant disabilities which sometimes attend its application and those occasional accidents which may be so shocking as to

"... milk the heart out of a man and shame him before his kind" (Rudyard Kipling).

Speaking for myself, I cannot agree with those who give the impression that they themselves would be content to supplant the normal mechanism by this short cut—a faith which I have heard preached from this platform.

Let me once again reiterate my position with regard to this whole matter as I should be greatly distressed if, with a certain amount of experience behind me, I was quoted as lending the authority of years to general approval of a more limited operation for some types of malignant disease of the lower bowel. As I said on a previous occasion (*Acta Chir. Scand.*, 1932, 72, 519) I make no extravagant claims for these operations nor do I speak of them in any sense of general advocacy. For years I have been almost afraid to mention them lest any word of mine should help to put back the clock of surgical progress. The most I wish to convey is my honest feeling that in view of the great advantage to the patient these operations deserve the attention of earnest workers in proctology.

Professor Charles A Pannett: There can be no difference of opinion as to the revolting nature of a colostomy. No patient likes it, many become resigned to it and adapt themselves to an unfortunate situation; to some it is a calamity. In many cases of carcinoma of the rectum it can be avoided. The question is, however, whether the retention of a controllable sphincter is compatible with effective removal of the growth. I am not able to base an affirmative answer to this question on a statistical survey as the number of cases I have operated upon is not great enough to be significant for this kind of analysis. Yet all my experience points to conservative resection as frequently not only desirable but sufficient.

For many years surgery of malignant disease of the rectum has been dominated by the personality of that brilliant surgeon Ernest Miles. We accepted without demur his conclusions based upon his careful, painstaking and accurate observation. But in these deductions he was in error. It is perfectly true that in advanced cases of carcinoma of the rectum and in post-mortem examinations in this disease, the spread of the growth may be demonstrated downwards and laterally into the ischio-rectal space. But when it is possible to remove the growth surgically this is rarely the case. The credit for pointing out this must be given to Westhues. It was in 1930 that he first published his observations. His important monograph appeared in 1934. The most painstaking dissections of 74 operation specimens was undertaken. In brief, he demonstrated beyond doubt that spread is mainly upwards into the glands around the superior hemorrhoidal vessels. Only once in all these examples did he find extension beyond 1 cm. below the naked-eye margin of the growth. In the upward direction the spread in the wall of the bowel was a little more extensive, but in the tissue

THE ANTERIOR OPERATION

The other method which I have pursued is an upper conservative operation (i.e. conservation of the sphincter apparatus) which might perhaps be better named "anterior resection with restoration of continuity and preservation of the sphincters". I was first led to consider this idea by an early experience concerning a neglected large bowel obstruction in a man of 55. He was short, fat and alcoholic and it was only when survival had been despaired of that a life-saving cæcostomy changed the whole picture. Later on exploratory laparotomy disclosed a constricting carcinoma in the first part of the rectum almost flush with the bottom of the rectovesical pouch. It was difficult to expose but I managed to divide the bowel across just below the growth and to remove it with about a foot of bowel above. The operation was completed by closing the rectal end, making a terminal colostomy and repairing the cæcostomy. This man made an excellent recovery and to my astonishment after so inadequate an operation for cancer, he lived in good health for seven years when he died probably from secondary deposits in the liver, although there was some discussion as to whether it was not from alcoholic cirrhosis of the liver which he had most certainly earned.

Another thought-provoking case was that of a very stout woman with a growth on the lowest part of the pelvic colon and first part of the rectum. I was just able to divide the peritoneum around the growth and to cut the rectum across close below it and to tuck in the lower end. The affected part, with a sufficient length of bowel and corresponding mesentery, was then removed and the operation completed by a terminal colostomy. The lantern slide shows the enormous amount of fat with which one had to contend and I freely admit it would have been extremely difficult to make an anastomosis. To my astonishment this patient continued to keep well and nineteen years later was in excellent health without any suspicion of recurrence. Experiences such as these certainly encouraged the preservation of the lower rectum with restoration of continuity of the bowel.

The general technique of this anterior method is very straightforward, though difficult, especially when it is employed for examples of rectal growth rather than those which are situated about the termination of the pelvic colon.

I would always advise a preliminary exploration through a median incision to determine beyond all question that the case is suitable for the anterior resection with restoration. This is combined with a temporary colostomy of the dysfunctioning type which may be iliac or transverse. The lower segment of the bowel should be thoroughly emptied and cleansed by irrigation but the latter should be neither too frequent nor too vigorous as it may traumatize the growth or encourage dissemination. The mobilization and separation of the bowel above and in the vicinity of the growth, together with the removal of the lymphatic area, are made as in any of the combined operations but the exposure of a sufficiency of the rectum below the growth has to be carried out after incising the peritoneum circumferentially about 2.5 cm. from the bowel and then carrying on the separation amongst the cellular tissue into the depths of the pelvis between the levatores ani. When a suitable length of bowel below the growth has been exposed (I usually aim at 5 cm.), the bowel is divided, usually with right-angled scissors but without the use of clamps as I find it impossible to apply them in this situation without their getting very much in the way and they are really quite unnecessary. One has to take great care that the division of the bowel is not too oblique and of course any vessels must be picked up and tied as they are divided. The actual anastomosis is then made by direct suture using first a series of mattress guide sutures and then a continuous circular suture which may be applied just for convenience in two or more sections. In the presence of a satisfactory dysfunctioning colostomy I have not thought it essential to attempt a watertight union but, of course, so far as possible, the mucous membrane should be inverted. In all such cases the union is well below the level of the peritoneum and lies among the vulnerable cellular tissue. That being so, it is a relief to be able to use one of the penicillin powders as an additional safeguard. I have not systematically used a tube passed from the anus to a point above the level of the anastomosis though this may have advantages. It is most important that the end of any such tube should not actually rest against any part of the bowel, where it might cause pressure necrosis. Personally, when I omit such a tube a blunt-ended tube is left *in situ* just above the sphincter or a rectal tube is passed through the sphincter at least twice daily for about four days. This manœuvre is much less uncomfortable for the patient than the continuous wearing of a tube through the anus. I have never ventured to close the abdomen without some type of drain brought from the cellular tissue and out of the lower end of the abdominal incision but it may be feasible and advisable in these days of chemical prophylaxis. If union is going to be a success it should be secure by the end of a fortnight but I have not cared to risk closure of the colostomy sooner than the end of three weeks and must admit that this stage has sometimes been followed by a temporary faecal fistula in the lower end of the incision. Closure must not be deferred for too long as there is a risk of an obliteration at the site of the anastomosis which occurred in one of my cases. The

Operating from above, the surgeon is cramped by the narrow space in which he has to work. It is not possible to use clamps and some contamination must occur. Sulphathalidine for forty-eight hours before the operation and 250,000 units of penicillin immediately following it are some help. But if the immunity of the patient be high—a fact we cannot tell—good results are obtained without their aid. Equally, if his resistance happens to be low, serious, perhaps fatal, sepsis may follow. It is of some help to fix the two ends of the bowel behind by three cotton sutures which are all inserted and left loose before any are tied (fig. 3). The posterior line of the suture can then be completed. The anterior aspect is more easy to deal with. Provided the mucous membrane is accurately turned in everywhere, union takes place well, but the junction is not an easy one to make; there is a lot of tissue behind the stump difficult to deal with and the two ends may not be of equal calibre. The technical resources of the surgeon are called upon. Whilst I have operated upon a number of patients by the abdominal route without drainage, I think it better to have a drainage tube in the hollow of the sacrum passing upwards beneath the sigmoid to emerge in the left iliac fossa from a hole of its own (fig. 4). From this tube a most foul discharge will come away for

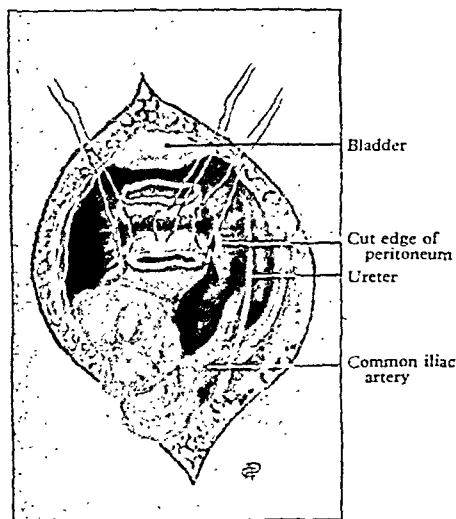


FIG. 3.—The insertion of the first fixation sutures.

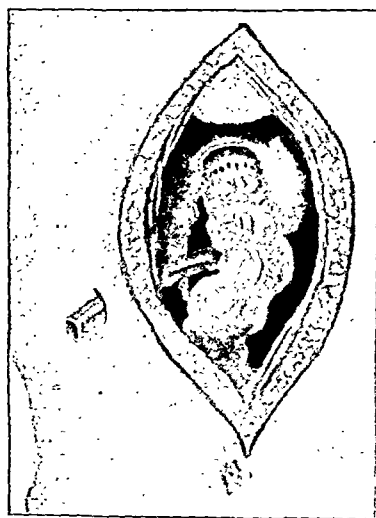


FIG. 4.—Completion of the anastomosis and the placing of the drainage tube.

forty-eight hours and then often suddenly dry up. I remove the tube after four days. I also prefer to leave a tube in the rectum reaching up above the site of the anastomosis. Often this has been omitted without ill-result but in one patient intestinal obstruction came on and was only relieved by the passage of the tube. With the wholly abdominal operation there is little disturbance of the patient. Leaving the pelvic floor intact seems to lessen the shock considerably. For these reasons even if it is impossible to bring the colon down to the rectal stump I leave the pelvic diaphragm and the sphincters.

When the growth is too low to do the whole operation from above, the separated bowel is pushed down into the hollow of the sacrum, the cut peritoneum sutured to its sides and the abdomen closed. The junction is then made after excising the coccyx. I described the technique of this operation in 1935 (*Lancet* (ii), 43). Whilst the whole of the coccygeus is divided, as little as possible of the levator ani is cut and the incision made as close to the rectum as possible in order to preserve the nerve supply of the rectal stump and the bladder. In separating the rectum from the prostate in front one must be sure to cut through the visceral pelvic fascia or one may find oneself too far forward in the prostatic plexus of the veins. I always seem to get some leakage when making the anastomosis from below but I have never had a persistent fistula.

Liquid paraffin is given daily for fourteen days after the operation, but should not be persisted in too long. Patients must not get into the habit of taking liquid paraffin. In two cases troublesome strictures occurred at the site of the anastomosis because of this. When the paraffin was stopped and they began to pass solid faeces the strictures soon opened up.

behind the rectum it extended up to 10 cm. or exceptionally 12 cm. above the growth. Laterally spread did not occur. Locally there was apt to be a break-through behind, and in front the rectovesical pouch was sometimes invaded. Both of these happenings are of serious import, but not, as I can vouch, incompatible with lasting cure. Dukes, Gabriel and Bussey (*Brit. J. Surg.*, 1935, 23, 395) support these views. In only two of those dissections depicted were infected paracolic glands shown below the growth and these are very close to its margin. These observations show that the wide removal of tissue laterally and below a growth of the rectum, as advocated by Miles, is unnecessary and unwarranted by the facts.

In a malignant growth of the rectum, the growth itself should be removed with two centimetres of normal rectum below its margin, and also 22 cm. of the rectum above its upper margin, because here there may be undischarged polypi, the forerunners of carcinoma, and all the tissue behind the bowel surrounding the superior hæmorrhoidal vessels upwards for 12 cm. This allows of the inferior mesenteric artery being tied at such a place that the blood supply of the sigmoid loop is preserved, and, if the loop is of ordinary length, sufficient is left to reach the stump of the bowel below.

The technical problem of joining the two ends of the severed gut is not a simple one. It can be accomplished either wholly from above, or if the stump of the rectum is very short, from behind after removing the coccyx. In both cases, by simple methods of suturing, perfectly controlled evacuation can be preserved. Unless this can be done the added risks of infection associated with conservative resection are not worth taking. The patient would be better off with an iliac colostomy. Pull-through methods or those necessitating division of the sphincter posteriorly, or any method requiring removal of the anal mucosa, all lead to imperfect control and should be discarded. Fig. 1, picture of a dissected fœtus, shows how intricate is the nerve supply of the rectum, anal region and bladder. The plexus of nerves is more complex than shown there, many fibrils being too fine to preserve. Physiological investigation shows that control depends upon the parasympathetic supply. Damage to the extrinsic sympathetic nerves does not lead to loss of control. This is fortunate from a surgical point of view. The nerves of the sacral plexus are preserved from damage in freeing the bowel from the hollow of the sacrum by the parietal layer of the pelvic fascia. In separating the

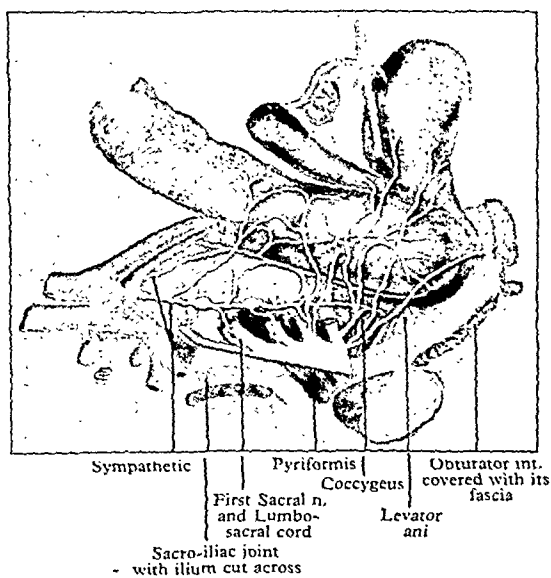


FIG. 1.—Dissection of infant's pelvis from side.

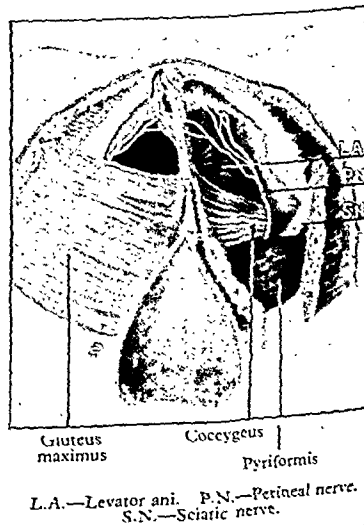


FIG. 2.—Dissection of perineal aspect of rectum in infant.

connective tissue here the fascia must be very closely adhered to, otherwise dangerous tissue may be left behind. Nerve branches which perforate this fascia to go to the rectum, as the sympathetic branches do, are necessarily ruptured. The important parasympathetic branches from S3 and S4 are deep to the rectovesical fascia and are in no danger when the whole pelvic diaphragm is preserved in the upper method of restoration. When, however, the junction is made from below there is some risk of harm being done. To avoid it the coccygeus should be divided close to the bone and as little as possible of the levator ani cut, the incision here being close to the rectum. The position of the nerves as seen from behind is shown in fig. 2.

operations. It is difficult for the pathologist examining operation specimens to evaluate the importance of excising these structures since they are normally in some degree of tension and after division they collapse and become misplaced.

Another point with regard to the radical removal of annular or anteriorly placed growths of the lower half of the rectum in females is the necessity to remove the posterior vaginal wall as a routine in order to reduce the possibility of vaginal recurrence; this of course is incompatible with any restorative procedure. The pathological findings of Dukes, David, Gilchrist and others indicate that it is necessary to divide the bowel and its mesentery at least 4 to 5 cm. below the lesion.

In the transabdominal restorative operation the division and removal of an adequate amount of mesorectum for growths in the lower half of the rectum offers difficulties. The mesorectum can be regarded as a cone and it will be seen from the accompanying diagrams (fig. 1) that the upper mesorectum is relatively narrow and a wide excision can be accomplished.

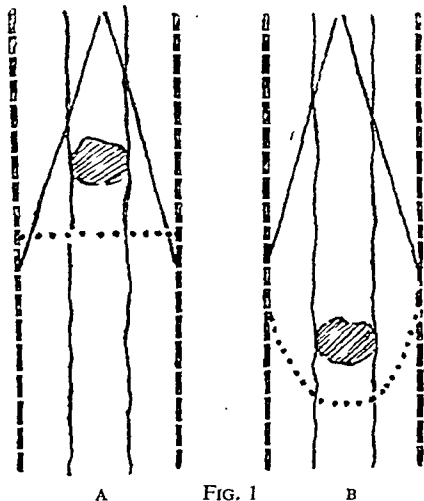


FIG. 1

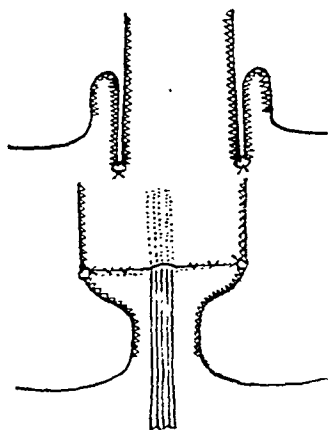


FIG. 2.

FIG. 1A.—Diagram of growth in the upper half of the rectum showing complete removal of all the mesorectum 4-5 cm. below the growth.

FIG. 1B.—Diagram of growth in the lower half of the rectum showing inadequate removal of mesorectum.

FIG. 2.—Diagram of anastomosis in abdomino-anal excisions showing drainage of presacral space through the posterior part of the anastomosis.

In the lower half of the rectum the mesentery is much broader and to divide it adequately below the growth on a broad base in the depths of the pelvis is a difficult procedure. The surgeon is often forced to indulge in a whittling process, particularly in a narrow pelvis, in order to define the bowel before division.

For these reasons growths of the lower half of the rectum, that is, growths which can be easily felt with the finger, growths which are below the peritoneal reflexion, cannot be as radically dealt with by restorative methods and should be excluded unless the growth is particularly suitably placed and extremely early. Tumours in the upper half of the rectum at or above the peritoneal reflexion which, as a rule, can barely be felt with the tip of the finger, may in general be regarded as suitable but other factors such as a short pelvic loop or diverticulitis may diminish the number of cases in which a restorative operation can be performed.

Operation methods.—With regard to the methods I shall briefly describe those which we have used. In the first place the anal canal musculature and its sensitive lining must be retained intact if proper control and continence are to be maintained. All the methods which involve the removal of anal mucosa and its replacement by colon mucosa, or in which the anorectal ring is divided, merely result in giving the patient a perineal colostomy. Secondly, for the very reasons that the combined excision has superseded the perineal excision, no perineal approach alone can be adequately radical. In our series of restorative cases at St. Mark's we have performed three types of operation: (1) abdominosacral excision in which the whole dissection is from above and the anastomosis performed through a parasacral or perineal incision; (2) abdomino-anal excision: here again the whole dissection is from above, the anastomosis being performed outside the anus by invaginating the remaining cuff of

Convalescence after the coccygeal anastomosis takes weeks longer than if everything is done above, but the ultimate result is just as satisfactory.

One other question arises. Is it necessary to make a preliminary colostomy? In the presence of a pronounced obstruction it is advisable; but colostomy should be avoided if possible, as almost certainly there will develop a fibrous stricture at the site of the anastomosis which will remain, in spite of fortnightly digital dilatation, until it is subjected to the daily passing of solid faeces.

I have lived to see demonstrated the hollowness of cherished surgical beliefs—to see the indestructible atom shattered into fragments—so that I have come to feel that scientific advance can be made only if we regard our contemporary beliefs as always wrong, or at most only half-truths. But when I remember, in connexion with the conservative resection operation, patients living twelve and thirteen years in normal health, unaware that they have a rectum, except for a satisfactory reminder once a day, I am tempted to place the foundations on which the conservative operation is based amongst the dependable half-truths.

Mr. O. V. Lloyd-Davies: It has always been one of the goals of the surgeon to be able to remove rectal growths without the necessity for a permanent colostomy and many attempts have been made over the course of years. In the past, sepsis, both local and general, was such a predominating factor that it gave rise to a mortality rate which forbade the general use of these methods and hence it was never possible to study the end-results. In 1887, Shede performed a preliminary colostomy before resecting a tumour posteriorly and restoring continuity but this very advisable step was never popularized. In later years, surgeons tended to rely upon a caecostomy to act as a vent and reduce gas tension, and upon tubes passing through the anastomosis, since it was realized that increased gas tension or activity of the anastomosed gut might be the all-important determining factors in success or failure.

Few considered the advisability of a preliminary transverse colostomy and although this procedure has since been criticized for various reasons, it was a distinct advance towards safety in restorative operations. There have been no deaths from sepsis at St. Mark's since a preliminary transverse colostomy has been used; I refer of course to cases performed before the discovery of the bowel sulphonamides. Milligan in 1926 was the first at St. Mark's to use a preliminary colostomy before resection and in 1935 Devine made a good case for a preliminary transverse colostomy.

Since the advent of the sulphonamides, more particularly sulphasuxidine and sulphathalidine, there has been a renewed and increasing trend towards attempting restorative resections for cancer of the rectum and rectosigmoid. The wave of enthusiasm has been so forceful, that in reading the surgical literature of some countries one might almost be persuaded that these restorative operations were the operations of choice and that all the older-established combined operations had had their day.

The development of sound methods for accomplishing these restorative operations is very desirable but a long view must be taken and at this stage it is worth while analysing the objectives which one hopes to attain. In assessing our work on rectal cancer we have a yardstick with which to check the results of new developments. This is the combined excision operation first developed by that great surgeon, Ernest Miles, who planned the abdomino-perineal operation in 1908. To-day there are various other forms of combined excision, the perineo-abdominal operation of Grey Turner and Gabriel and the synchronous combined excision, and we know from the figures of many clinics that a 50% five-year cure rate is the best that can be obtained by surgery and that only earlier diagnosis will improve this figure in any substantial way.

The first objective in restorative operations must therefore be long-term results which are as good as those of combined excision operations. We are not entitled to take risks with the growth or the patient merely to avoid a colostomy and restore continuity. The restorative operation must be as radical as a combined excision.

Upper limits.—The upper limit of division of the inferior mesenteric vascular and lymphatic trunks in a synchronous combined excision is immediately below the left colic artery in two-thirds of the cases and below the first sigmoid artery in the remaining third. This should be the criterion for restorative operations but since a greater length of colon has to be retained this may not always be possible and an additional strain is placed on the acumen of the surgeon who has to judge whether his operation is still as radical as it should be. In some cases this difficulty can be overcome when the middle colic vessels are sufficiently long to allow the transverse colon to be anastomosed to the rectum.

Lower limits.—There is no lower limit in a combined excision operation. It is a wide removal of all the tissues surrounding the lower half of the rectum including the greater part of the levators and the rectal fascia of Waldeyer. The fascia of Waldeyer and the broad pubo-coccygeus portions of the levator are in intimate contact with the lower half of the rectum and must have a definite lymphatic significance; they are not removed in restorative

operations. It is difficult for the pathologist examining operation specimens to evaluate the importance of excising these structures since they are normally in some degree of tension and after division they collapse and become misplaced.

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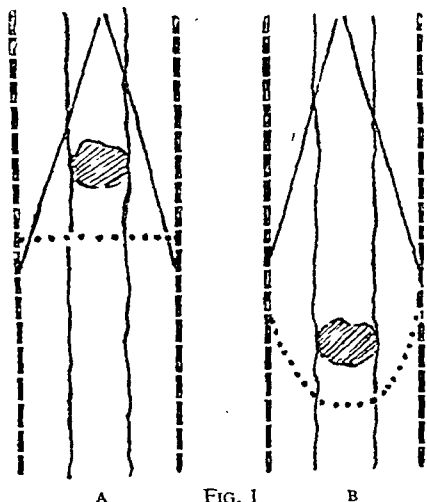


FIG. 1.

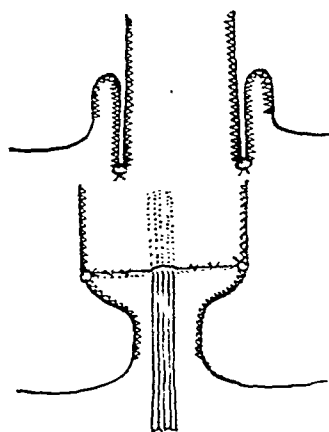


FIG. 2.

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rectum and joining colon to rectal cuff as in the rectosigmoidectomy operation; (3) entirely transabdominal resections.

Lower pelvic colon growths naturally come into this series and we decided to include only those in which the growth was too low for a Paul-Mikulicz operation to have been performed.

These operations have been done in one, two and three stages, the three-stage operation being a preliminary laparotomy and transverse colostomy followed by a resection operation and later extraperitoneal closure of the colostomy. In the two-stage operation a temporary transverse colostomy is performed at the end of the operation and closed at a later stage.

Complications.—The earliest cases in the series were abdominosacral operations and this operation was abandoned owing to the development of a fistula between the anastomosis and the perineal or sacral wound. These were all three-stage operations and because of delay in closure of the fistula the transverse colostomy had often to be retained for a considerable time. In no case was the fistula permanent.

Our method of abdomino-anal excision was devised to overcome this difficulty, the presacral space being drained *per anum* through the posterior part of the anastomosis (fig. 2); this permitted an earlier closure of the colostomy.

In both these operations some narrowing at the site of anastomosis has been frequent. This has been due to anastomosing the narrow colon to the wide lower cuff of rectum. In those cases in which there has been enough length of colon to divide it sufficiently obliquely, no strictures have developed. These operations require a greater length of bowel than the entirely transabdominal resections.

Sepsis.—To ascertain how the battle of sepsis is progressing let us examine the entirely transabdominal or intraperitoneal resection series, all of which had a preoperative five-day course of either sulphasuxidine or sulphathalidine. There have been seven cases, approximately 25%, with temporary complications in association with the anastomosis.

TABLE I

Complications (7 cases)

- (1) Posterior separation, pelvic cellulitis
- (2) Colo-vaginal fistula
- (3) Posterior separation with abscess
- (4) Posterior separation and colo-vaginal fistula
- (5) Faecal leak along pelvic drain
- (6) Faecal leak along pelvic drain
- (7) Para-rectal abscess

All of these cases have probably been due to some partial deficiency in the blood supply to the junction and there is no doubt that more serious complications as the result of this defect have been prevented by pre- and post-operative chemotherapy. These complications have been more common in the one-stage operations but in no case has permanent trouble resulted.

The two-stage operation in which a transverse colostomy is performed at the completion of the resection appears to offer a greater measure of safety to the patient than the one-stage operation should any complication occur.

With regard to the three-stage operation, this may now only be necessary when it has been impossible to empty the colon adequately before operating.

Blood supply.—Regarding the blood supply a decision has to be made as to whether or not the descending branch of the left colic artery will adequately supply a sufficient length of bowel. If this vessel appears to be large and suitable a further test can be made by compressing the main inferior mesenteric trunk and noting at what point arterial pulsation ceases on the bowel wall. If this length of bowel is not sufficient the first sigmoid artery will have to be retained. Further length of vascular bowel can be obtained by dividing the remaining sigmoid arteries proximal to their arcades (figs. 3 and 4). Viable bowel is determined by its colour, pulsating arterioles and finally by free bleeding from the divided end.

The majority of these transabdominal pelvic anastomoses have been of the open end-to-end type and in this connexion it must be remembered that whilst accurate anastomosis is all-important, excessive suturing will devitalize the end blood supply.

It is important to make division of the two opposing ends of bowel as oblique as possible. To obtain full advantage of the length of the pelvic loop the mesenteric border of the colon can be applied to the antimesenteric surface of the rectal stump and vice versa. This rotates the colon slightly but does not twist the mesentery and has the additional advantage of uniting the most vascular borders to the least vascular borders and makes for greater safety. There have been no complications in using this method. The site of the anastomosis should always be drained.

End-results.—In the three methods which we have used we have tried as faithfully as possible to be as radical as in a combined excision. The majority of the tumours have been at or above the peritoneal reflexion. The average height of the lower border of the growth in the abdomino-anal and sacral series is 11.5 cm. and in the intraperitoneal resection series

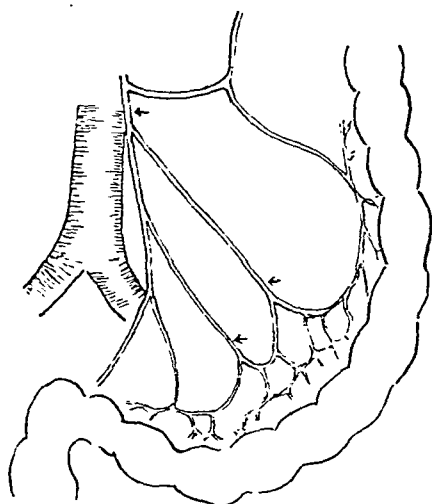


FIG. 3.—Diagram to show the usual arrangement of sigmoid vessels.

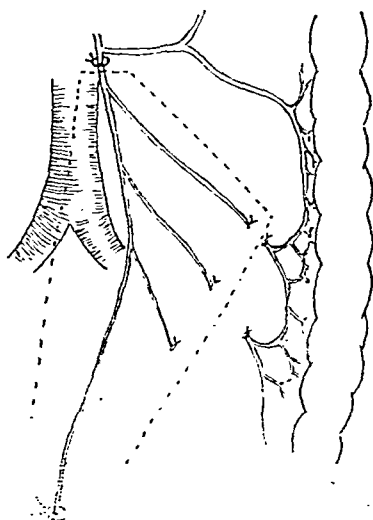


FIG. 4.—Diagram to show division of sigmoid vessels proximal to their arcades to obtain maximum length of viable bowel. The dotted line indicates the amount of tissue removed.

13 cm. The average distance of free bowel and mesentery below the lesion has been 1.8 and 1.5 in. (4.5 and 3.8 cm.). In half the intraperitoneal cases the anastomosed proximal colon has been supplied by the descending branch of the left colic and in the remaining half the first or second sigmoid arteries have been left as a supply.

TABLE II.—ABDOMINO-ANAL AND ABDOMINO-SACRAL CASES

Total 24, including 3 Bacon-Babcock operations

Death 1 (eighth post-operative day) Cause = Bronchopneumonia

Average distance of free bowel below growth 4.5 cm.

Average height by sigmoidoscopy

11.5 cm. { lowest 8 cm.
highest 18 cm.

Dukes' classifications

3 stage operations 20

A cases 10

2 stage operations 1

B cases 4

1 stage operations (B.B.) .. 3

C cases 10

TABLE III.—INTRAPERITONEAL RESECTION CASES (Too Recent for Follow-up Purposes)

1 Suture Line Recurrence to Date

Total 30 (To December 1947)

Deaths 2 1 aged 70. Cause : hæmorrhage and shock

1 aged 52. Cause : perforated gastric ulcer 19th day

(No deaths from sepsis)

Average distance free bowel below growth 3.8 cm.

Average height by sigmoidoscopy

13.0 cm. { lowest 7 cm.
highest 25 cm.

Vessel Left to Supply Colon

Descending branch left colic artery

15 cases

First or second sigmoid artery

15 cases

Dukes' classifications

3 stage operations 13

A cases 3

2 stage operations 9

B cases 9

1 stage operations 8

C cases 18

rectum and joining colon to rectal cuff as in the rectosigmoidectomy operation; (3) entirely transabdominal resections.

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In considering the above possibilities it is particularly disturbing to observe that four A cases have developed local recurrences. To compare with this the A cases in a series of combined excisions of over five years' duration were examined and of 54 cases none had developed local pelvic recurrences.

Lastly, distinct second primary tumours developing away from the anastomosis.

A local recurrence rate of 24.6% is too big a price to pay for avoidance of a permanent colostomy. Death from local recurrences is always a miserable ending.

The final figure may be worse since a half of the cases have yet to run a complete five-year course and a second primary may arise at any later date.

We have performed secondary excision operations for a number of these recurrences but our experience is that these second operations are always troublesome since the normal tissue planes no longer exist, the growth does not spread along the normal channels and it is often difficult to distinguish fibrous tissue from growth.

If in view of the present greater safety in performing these restorative operations they are to have a permanent place in the treatment of rectal cancer then the end-results will have to be considerably improved.

Growths of the lower half of the rectum below the peritoneal reflexion must be excluded. There should be an adequate removal of tissue and division of the bowel and its mesentery at least two inches below the tumour.

Especial care must be taken to avoid implanting cancer cells. We at St. Mark's have been aware of this danger for some time and have adopted the following plan when performing restorative resections.

A clamp is applied to the bowel at least 2 in. below the growth and the distal portion is irrigated through the anus with 1 : 1,000 perchloride of mercury. The bowel is then divided, the distal portion being held with tissue forceps or stay sutures. To complete the toilet perchloride swabs followed by dry swabs are pushed down to the anus where they are removed by an assistant.

Since the patients are always placed in the lithotomy-Trendelenburg position this manœuvre is a simple matter.

It is too early to give any statistics which will prove whether this method is effective in reducing local recurrence due to implantation.

My impressions are that results will be improved now that we are aware of this danger and are taking steps to combat it.

A very close follow-up must be kept upon these patients and this means rectal examination by palpation and sigmoidoscopy three-monthly and later six-monthly and then yearly for the rest of their lives. It will be necessary in a few years' time to make a complete review of these cases; meanwhile restorative operations must be as radical as possible always bearing in mind the grave risk of local recurrence and taking every precaution to prevent it.

[July 14, 1948]

MEETING AT THE GORDON HOSPITAL, VAUXHALL BRIDGE ROAD, LONDON, S.W.1

Two Cases by ERIC A. CROOK, M.Ch.

I.—Sarcoma Discovered in Hæmorrhoid after Ligature Operation.

E. J. H., aged 40.

Ligature operation for hæmorrhoids, one of which was excised on account of its size and microscopic examination showed sarcoma.

The problem was whether radical treatment should be adopted.

The opinions expressed were that in view of the hæmorrhoid having been completely removed, the patient should be kept under observation and further operative measures carried out if there were any evidence of local recurrence.

II.—Urethral Fistula Following Abdominoperineal Excision of Rectum.

W. E. U., aged 59.

Abdominoperineal excision of the rectum on 15.10.47. Growth $3 \times 2\frac{1}{2}$ cm. Microscopically Grade II malignancy (Broders') and Class B case (Dukes').

Wound was slow in healing and a urethral fistula persisted. The latter has healed and broken down periodically, otherwise his condition has been entirely satisfactory.

The problem was whether surgical measures should be adopted to make the fistula heal.

The views expressed were that the fistula would probably consolidate on its own, without operative treatment.

An analysis of this small series of 54 restorative cases done at St. Mark's gives the following results (Table IV); they are seriously disappointing. The bright side to the picture is the operative mortality of 5.5% with no deaths from sepsis or peritonitis. This compares with our mortality of 4.1% for Paul-Mikulicz operations. One-third of the cases were done before the days of the bowel sterilizing sulphonamides but these were all three-stage operations.

TABLE IV.—OPERATIVE MORTALITY FOR RESTORATIVE CASES

Abdomino-anal and abdomino-sacral ..	24	1 death
Intraperitoneal resections (transabdominal)	30	2 deaths
Total	54	3 deaths

Mortality rate 5.5%.

Of the 54 cases half of them are too recent for follow-up purposes and so to obtain a broader picture the results of 19 radical Hartmann operations were investigated, the palliative operations, that is those with known liver secondaries, being excluded. In these Hartmann operations the bowel is divided in much the same way as in restorative operations and there remains an invaginated rectal stump which provides a somewhat similar state of affairs to study.

If these figures be all grouped together and all palliative operations are excluded a total of 65 cases is obtained made up of: 23 abdomino-anal and sacral; 23 intraperitoneal or transabdominal resections, and 19 Hartmanns and to date 16 have developed a local pelvic recurrence (Tables V, VI and VII).

TABLE V

	Local recurrences
Abdomino-sacral and anal cases	
24—1 death = 23	9
Intraperitoneal resections	
30—2 deaths—5 palliatives = 23	1
Hartmann operations	6
Total 65	16

Percentage recurrence 24.6

TABLE VI.—ABDOMINO-ANAL AND ABDOMINO-SACRAL CASES

Local Pelvic Recurrences Occurring Between Six Months and Six Years after Operation

9 cases	Position of Recurrence	
A cases 2	Rectovaginal septum	3 cases
B cases 2	Suture line and drain track	3 cases
C cases 5	Insufficient data to determine initial site of recurrence ..	3 cases

TABLE VII.—HARTMANN OPERATIONS

Excluding palliative operations	19 cases
Local recurrences 6	
Recurrences at invagination	3 { 2 A cases 1 B case
Noted twelve, fifteen and eighteen months after operation	
Implantation	1 C case
Noted six months after operation	
Second primary growths	2 { 1 A case 1 C case
Noted two years and seven years after operation	

There have been recurrences at the suture line, drainage track implants and second primary carcinomata. This gives a local recurrence rate of 24.6%, which is a serious matter. There are several possible explanations:

First, inadequate removal of the primary tumour, in other words failure to carry out the criteria which have been just described for performing a radical operation.

Secondly, implantation of cancer cells at the time of the operation. We know that this can occur as we have instances of adenocarcinomata developing at the external openings of fistulous tracks, there being no direct continuity with the primary tumour in the bowel.

Thirdly, a traumatic factor caused by the suturing may, as experimental work on cancer has shown, result in the stimulation of rectal epithelium which has a predisposition to producing malignant change. Quite a number of these recurrences have occurred in the rectal rather than colonic side of the anastomosis.

In considering the above possibilities it is particularly disturbing to observe that four A cases have developed local recurrences. To compare with this the A cases in a series of combined excisions of over five years' duration were examined and of 54 cases none had developed local pelvic recurrences.

Lastly, distinct second primary tumours developing away from the anastomosis.

A local recurrence rate of 24.6% is too big a price to pay for avoidance of a permanent colostomy. Death from local recurrences is always a miserable ending.

The final figure may be worse since a half of the cases have yet to run a complete five-year course and a second primary may arise at any later date.

We have performed secondary excision operations for a number of these recurrences but our experience is that these second operations are always troublesome since the normal tissue planes no longer exist, the growth does not spread along the normal channels and it is often difficult to distinguish fibrous tissue from growth.

If in view of the present greater safety in performing these restorative operations they are to have a permanent place in the treatment of rectal cancer then the end-results will have to be considerably improved.

Growths of the lower half of the rectum below the peritoneal reflexion must be excluded. There should be an adequate removal of tissue and division of the bowel and its mesentery at least two inches below the tumour.

Especially care must be taken to avoid implanting cancer cells. We at St. Mark's have been aware of this danger for some time and have adopted the following plan when performing restorative resections.

A clamp is applied to the bowel at least 2 in. below the growth and the distal portion is irrigated through the anus with 1 : 1,000 perchloride of mercury. The bowel is then divided, the distal portion being held with tissue forceps or stay sutures. To complete the toilet perchloride swabs followed by dry swabs are pushed down to the anus where they are removed by an assistant.

Since the patients are always placed in the lithotomy-Trendelenburg position this manoeuvre is a simple matter.

It is too early to give any statistics which will prove whether this method is effective in reducing local recurrence due to implantation.

My impressions are that results will be improved now that we are aware of this danger and are taking steps to combat it.

A very close follow-up must be kept upon these patients and this means rectal examination by palpation and sigmoidoscopy three-monthly and later six-monthly and then yearly for the rest of their lives. It will be necessary in a few years' time to make a complete review of these cases; meanwhile restorative operations must be as radical as possible always bearing in mind the grave risk of local recurrence and taking every precaution to prevent it.

[July 14, 1948]

MEETING AT THE GORDON HOSPITAL, VAUXHALL BRIDGE ROAD, LONDON, S.W.1

Two Cases by ERIC A. CROOK, M.Ch.

I.—Sarcoma Discovered in Hæmorrhoid after Ligature Operation.

E. J. H., aged 40.

Ligature operation for hæmorrhoids, one of which was excised on account of its size and microscopic examination showed sarcoma.

The problem was whether radical treatment should be adopted.

The opinions expressed were that in view of the hæmorrhoid having been completely removed, the patient should be kept under observation and further operative measures carried out if there were any evidence of local recurrence.

II.—Urethral Fistula Following Abdominoperineal Excision of Rectum.

W. E. U., aged 59.

Abdominoperineal excision of the rectum on 15.10.47. Growth $3 \times 2\frac{1}{2}$ cm. Microscopically Grade II malignancy (Broders') and Class B case (Dukes').

Wound was slow in healing and a urethral fistula persisted. The latter has healed and broken down periodically, otherwise his condition has been entirely satisfactory.

The problem was whether surgical measures should be adopted to make the fistula heal.

The views expressed were that the fistula would probably consolidate on its own, without operative treatment.

Eight Cases by RONALD W. RAVEN, O.B.E., F.R.C.S.

I.—Carcinoma of Rectosigmoid Colon with Hepatic Metastases. Partial Colectomy and Insulin Therapy.

Female, aged 43, married with three children, noticed abdominal colicky pain in 1944. In July 1947 an exploratory laparotomy was performed by another surgeon who found a carcinoma at the rectosigmoid junction with metastases in the right lobe of the liver. The condition was pronounced inoperable and a left inguinal colostomy was established. The patient became aware of her condition and her husband and she were most anxious that an attempt should be made to eradicate the disease. On examination the patient was very thin, the liver was just palpable and there was a left inguinal colostomy with a spur. On rectal examination the lower margin of a carcinoma was felt.

Investigations: R.B.C. 3,190,000; W.B.C. 5,800; Hb 74%; blood urea 22 mg.%; plasma proteins, chlorides and ascorbic acid within normal limits. X-ray chest—no metastases.

Operations (Mr. R. W. Raven).—(1) on 1.10.47: Exploratory laparotomy revealed three metastases, 5 cm. in diameter, in the anterior and posterior aspects of the right lobe and Spigelian lobe of the liver. The left lobe appeared normal. Aortic lymph nodes not enlarged. An operable carcinoma was present at the rectosigmoid junction; partial colectomy was performed with closure of the two open ends of the colon. (2) on 29.10.47: The abdomen was reopened with the object of performing a partial right hepatectomy; the right lobe of the liver was mobilized but it was not possible to proceed further on account of the poor general condition of the patient.

She recovered from the operation but her condition continued to deteriorate, with loss of weight and anorexia. The use of a growth inhibitor substance was considered but not adopted. Mr. S. O. Aylett suggested insulin therapy and it was decided to give the patient 15 units t.d.s. In a short time a very marked improvement occurred; she became ravenously hungry and it was difficult to appease her appetite. She lost her depression and lethargy, became alert and had an intense interest in living.

Follow-up examination (14.7.48).—The patient is very well, with a good colour, and is able to work hard looking after her home and three children unaided. She has gained 4 st. in weight. The appetite continues to be excellent, insulin therapy is maintained and there are no signs of spread of the disease; the lower margin of the liver is just palpable.

Comment.—The relationship between the pancreas and malignant disease has been the subject of a number of investigations and several facts have been elucidated. Hypertrophy of the islets of Langerhans has been found in human cancer and in tumour-bearing mice. Several workers have reported the presence of substances in tumours which are capable of lowering the blood sugar, but this has not received complete confirmation. The view was put forward that hypertrophy of islet tissue in the presence of malignant disease was a defence mechanism with the underlying supposition that insulin might exert an inhibitory action on the growth of a tumour. This view appears to be reinforced by the knowledge that carbohydrates administered orally or parenterally cause tumour growth and therefore a substance which produces hypoglycaemia would have the opposite action. There is experimental evidence that insulin does exert a growth-inhibitor action in certain forms of malignant disease; on the other hand, there are a number of reports of the failure of insulin to affect tumour-growth. When insulin therapy has been used in human cancer it has been pointed out that the dosage of insulin and amount of carbohydrate ingested must be regulated so that the critical level of hypoglycaemia is just avoided. A series of 16 cases with inoperable cancer was treated by Silberstein¹ and co-workers when it was noted that improvement occurred in the general condition and the growth of the tumour was arrested. It has been shown, however, that after insulin therapy ceased the growth of the tumour was rapid.

II.—Carcinoma of Rectum with Hepatic Metastases. Abdominoperineal Excision and Partial Hepatectomy.

Female, aged 52, had diarrhoea, bleeding from the rectum and loss of weight extending over a period of six months. On examination she was pale and thin. There was a large, nodular, hard swelling in the position of the left lobe of the liver. On rectal examination an ulcerating carcinoma of the rectum was found, the lower margin was 7.5 cm. from the anal verge, and it was somewhat fixed anteriorly.

Operations (Mr. R. W. Raven).—23.3.48: Abdominoperineal excision of the rectum. 20.4.48: Left hepatectomy—the whole of the left lobe of the liver was massively involved.

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—, French, J. and Révész, T. (1927) *Z. ges. exp. Med.*, 55, 78.

by metastases; the right lobe was clear. Microscopic examination showed adenocarcinoma of the rectum and liver.

Follow-up examination (14.7.48).—Patient is well; no sign of recurrence.

Comment.—The operation of left hepatectomy whereby the whole of the left lobe of the liver is excised is a feasible operation when metastases are localized to this lobe, the primary growth is operable and there are no other distant metastases.

III and IV.—Carcinoma of Rectum. Abdominoperineal Proctosigmoidectomy.

III.—Male, aged 34, had suffered from constipation, rectal bleeding and loss of weight extending over a period of five months. On examination he was thin and pale. There was an ulcerating carcinoma in the left lower quadrant of the ampulla of the rectum whose lower border was 7.5 cm. from the anal verge; freely mobile.

Operation (Mr. R. W. Raven).—18.11.47: Abdominoperineal proctosigmoidectomy. Eight days after the operation the bowels were opening normally. Faradic stimulation given to the anal sphincters.

Follow-up examination (14.7.48).—Patient is well. No sign of recurrence. He has good sphincteric control of faeces. There is some stenosis at the anosigmoid junction.

IV.—Male, aged 55, had suffered for seven years with soreness at the anus, recurrent attacks of rectal bleeding, and prolapsing internal hæmorrhoids requiring replacement. On examination his general condition was good. On rectal examination there were prolapsing internal hæmorrhoids. Sigmoidoscopy revealed a carcinoma situated 15 cm. from the anal verge, chiefly involving the anterior wall. Carcinoma confirmed by biopsy.

Operation (Mr. R. W. Raven).—26.1.48: Abdominoperineal proctosigmoidectomy. Several days after operation there was some sloughing of the sigmoid colon at the anus with infection and fever. It was decided to institute a transverse colostomy on 31.1.48.

Follow-up examination (14.7.48).—Patient is well. No sign of recurrence. Good healing of anal canal. Transverse colostomy working well. This was closed later and patient has good sphincteric control of faeces.

Comment.—The two patients were selected to show certain features of the results of the operation. In the first patient a stricture has developed but this does not appear to affect the bowel action and he has almost perfect control over the stools. Stricture formation often occurs after abdominoperineal proctosigmoidectomy. In the second patient the sigmoid colon which had been brought through the anus sloughed and in order to prevent further infection and pelvic cellulitis a transverse colostomy was instituted and the infective process subsided; the patient made a good recovery. If this condition occurs after the operation a transverse colostomy is very desirable.

The perineal part of the operation of abdominoperineal proctosigmoidectomy is carried out as follows, with the patient in the lithotomy position: After the usual toilet preparation an incision is made in the mid-line commencing at the tip of the coccyx and ending to the posterior border of the internal sphincter muscle of the anus. This incision is deepened until the fibres of the levatores ani muscles are seen and these are separated in the mid-line. The fascia propria is incised and the rectum and sigmoid are delivered into the wound. The levatores ani muscles are cut laterally from the rectum which is separated anteriorly from the urethra or vagina. The anorectal junction is identified and divided, the upper divided end of the anal canal is held in tissue forceps. The tape around the area of proved vascularity in the sigmoid is identified and the colon is divided 6 cm. distal to this; the growth is thus removed. The proximal end of the sigmoid is passed through the anal canal and the tape should be localized at, or distal to, the anal orifice. No sutures are used to anchor the bowel; appendices epiploicæ are not removed since they carry small nutrient arteries to the bowel. A saline compress is placed around the protruding bowel. The levatores ani muscles are sutured together in the mid-line with interrupted sutures of silk, care being taken not to compress the bowel and the rest of the wound is closed around a small rubber tube inserted into the presacral region. Several days after the operation the patient is instructed to exercise the anal sphincters; later faradic stimulation may increase their power of contractility. About the tenth post-operative day the protruding bowel is divided with the cautery at a point 2 cm. beyond the anal orifice providing the perineal wound has healed satisfactorily. The patient commences to have bowel actions about the fifth post-operative day and thereafter he is given a lubricant by mouth until these are regulated. Digital dilatation is carried out if the anus tends to constrict. After an interval of two months most patients have excellent sphincteric control of the anus with little or no soiling.

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On examination.—Before operation a ring of prolapse 1½ in. in length protruded through a completely lax sphincter giving the impression of being mucosa only.

Admitted to hospital on 1.6.48. Examination under spinal anaesthesia: No more rectal wall could be pulled down and vaginal examination revealed much scarring and adhesions between the cervix and the posterior vaginal wall.

Operation (7.6.48).—Thiersch operation. Steel wire inserted subcutaneously around the lower end of the anal canal and tightened to the diameter of the proximal interphalangeal joint of the index finger.

Bowels opened on the sixth morning after operation with some difficulty owing to the very big faecal result, otherwise uninterrupted convalescence with no recurrence of the prolapse.

Patient is now taking normacol daily and complains of no prolapse.

Present state on examination: On straining a small portion of mucosa is visible through the sphincter which has not completely recovered its tone, but has improved with the post-operative exercises.

Hirschsprung's Disease

By F. DOUGLAS STEPHENS, D.S.O., M.S.Melb., F.R.A.C.S.

THE purpose of this paper is to emphasize three features concerning the group of cases characterized by megacolon without obvious organic obstruction such as atresia or stenosis: First, the subdivision of this group into clinical types, secondly, a brief outline of the general features of true Hirschsprung's disease, and the differentiation of this condition from the subgroups, and thirdly, clinical evidence that spasm in the rectosigmoid region is present in true Hirschsprung's disease and is the cause of the obstruction.

From the miscellaneous group of cases suffering from severe constipation with idiopathic megacolon, the following two clinical sub-groups are apparent.

(1) *True Hirschsprung's disease.*—This is a congenital condition characterized by constipation and abdominal distension, commencing at or soon after birth. In this series the majority are boys. It occasionally has a familial tendency, and in one family in this series of 30 cases there were two boys afflicted with this condition. There is abdominal distension caused chiefly by the gradual dilatation of the sigmoid colon. Gas formation occurs presumably as a result of prolonged stagnation of faecal contents and large quantities of foul flatus are passed *per rectum*. There are visible peristaltic waves. The stools in this condition are characteristically small round pellets or thin ribands like toothpaste. Faecal accumulations occur in the sigmoid colon but these are not as a rule palpable in the abdomen owing to the gaseous distension. Rectal examination reveals a normal sphincter and rectum which is usually empty, except perhaps for a small pellet of faeces. Faecal matter in the sigmoid colon can be palpated through the rectal wall. In babies it may be possible to pass one's finger proximally into the rectosigmoid region which sometimes simulates a stricture as a result of the spasm of the wall of the bowel at this site.

Pain is not a feature of Hirschsprung's disease unless it is that caused by acute gaseous distension due to inability to evacuate the flatus.

Vomiting may occur in the presence of severe abdominal distension.

(2) *Chronic constipation.*—Although in some cases constipation of a mild nature may have been noted since birth it is usual to find that in this condition it becomes severe at a later date.

In a number of cases exciting causes such as psychological trauma, enforced rest in bed due to an illness, or a domestic disturbance in the family involving parental neglect, are considered to be factors which precipitate an attack of persistent constipation. Mental backwardness has been noted in some cases.

There is more emphasis on the constipation than on the abdominal distension in this condition. Banking up of hard faeces in the rectum and sigmoid produces virtually an incomplete intestinal obstruction. There is overflow incontinence of the faeces from the anus and the stools are characteristically large in diameter and size. Abdominal colic and painful defaecation are common. It has been observed in some cases that defaecation in the standing position is less painful to the child than in the normal posture. The pain of defaecation causes voluntary retention of faeces and further constipation.

On examination the abdomen is moderately distended, and faecal accumulations are readily palpable. Peristalsis is less in evidence. The signs of chronic abdominal distension such as flaring of the ribs and eversion of the umbilicus are more commonly absent. Rectal examination reveals hard large faecal accumulations readily palpable in a distended rectum. The sphincter may even be held slightly open by the pressure of faeces above.

V, VI and VII.—Rectal Incontinence. Reconstruction of Anal Sphincters.

V.—Male, aged 40, complained of rectal incontinence. Two years ago he had an operation for an anorectal fistula at another hospital and since that time he has had complete loss of sphincteric control. Patient had an anxious expression. There was marked scarring of the perianal region with loss of sphincteric control.

Operation (Mr. R. W. Raven).—19.1.48: Reconstruction of the anal sphincters. An elliptical incision was made around the posterior aspect of the anus and deepened until the levatores ani muscles were identified. These muscles were reconstructed in the mid-line with interrupted sutures of silk. The divided ends of the internal sphincter muscle were identified and this muscle was reconstructed with interrupted sutures of silk. The wound was closed.

Follow-up examination (14.7.48).—Patient looks well and has lost his anxious expression. He is now continent with no fecal leakage or discharge. Digital examination shows good sphincteric action of anal muscles.

VI.—Female, aged 50, complained of rectal incontinence. In 1928 patient had an operation for gastric ulcer and peritonitis at another hospital. Intestinal occlusion followed later and she was operated on elsewhere. Subsequently she had eight operations on the rectum for anorectal fistula, the last being four years ago. As a result of these operations the patient was absolutely incontinent of feces and had an enema daily in an endeavour to empty the bowel and relieve the incontinence, but with poor results. She was unable to leave her house and life was a burden to her. She was advised to have a left inguinal colostomy at another hospital but refused. She looked distressed and anxious. There was marked scarring in the perineum; the rectovaginal septum was fibrotic and there was no evidence of any anal sphincteric action.

Operation (Mr. R. W. Raven).—30.10.46: Reconstruction of the anal sphincters. The rectovaginal space was exposed through a longitudinal incision through the posterior vaginal wall, the flaps being dissected up laterally. The divided ends of the levatores ani and internal sphincter muscles were identified and reconstructed using interrupted sutures of silk. The posterior vaginal wall was then repaired. Later faradic stimulation of the anal sphincters was carried out.

Follow-up examination (14.7.48).—Patient looks extremely well, is happy and her expression has completely changed. She has perfect control of feces, no leakage, bowels open normally and she now lives a normal life. Digital examination of the anus shows good sphincteric action.

VII.—Female, aged 47, complained of rectal incontinence following an operation on the rectum in U.S.A. twenty-two years ago. An operation for rectal incontinence was performed in Paris four years ago without improvement. She had severe fecal incontinence and the bowels were opened up to ten times a day. Patient looked anxious. There was very poor sphincteric action of the anal sphincters with marked scarring around the anus especially in the rectovaginal septum.

Operation (Mr. R. W. Raven).—9.1.48:—Reconstruction of anal sphincters through an elliptical incision anterior to the anus. The rectovaginal space was opened up and the levatores ani and internal sphincter muscles were identified and reconstructed with silk.

Follow-up examination (28.2.48).—Patient feels well. There is no incontinence of feces, if there are not too fluid; she can hold flatus.

Comment.—These three patients, suffering from a severe degree of rectal incontinence following anorectal operations, demonstrate the value of the operation for reconstruction of the anal sphincters. The improvement in the mental outlook of these patients following operation was most impressive.

VIII.—Carcinoma of Anus. Teleradium Therapy: Twelve-year survival without recurrence.

Male, aged 57, had noticed a growth around the anus for seven months with a gradual increase in size. There was a papilliferous carcinoma surrounding the anus with palpable lymph nodes in both groins. Biopsy of growth showed a squamous-cell carcinoma. He was treated by teleradium to anus and groins, total dose 124,114 mg. hrs.

Follow-up examination (14.7.48).—No sign of recurrence.

Comment.—This is an example of the successful treatment of squamous-cell carcinoma of the anus by teleradium without colostomy; twelve-year survival without recurrence.

Prolapse of the Rectum—Treated by Thiersch Operation.—K. L. JAMES, M.S.

Female, aged 61. Prolapse of the rectum with loss of sphincter control for two years, dating from an operation for prolapse of the uterus treated by anterior and posterior colporrhaphy with amputation of the cervix.

It has been noted that a sigmoid colostomy when performed on a child with true Hirschsprung's disease functions normally and the troublesome offensive flatus ceases. Closure of the colostomy is often difficult owing to fistula formation, but when successful is associated with recurrence of all the symptoms and signs. It would appear, therefore, that the dilated and hypertrophied colon functions normally, and that the segment between the sigmoid and the anus is abnormal and produces the obstructive phenomena.

Finally, if a spinal anæsthetic is administered and the barium enema performed during this anæsthetic, the rectosigmoid spasmodic segment is seen to increase in diameter and lose its haustrations. Therefore, it is highly suggestive that true Hirschsprung's disease is an obstruction caused by spasm in the region of variable length demonstrated by X-rays as a relatively narrow segment connecting the dilated colon with the anus.

The course of chronic constipation.—Most of the cases of chronic constipation, including those showing the long dilated sigmoid loop and the terminal reservoir, have responded satisfactorily to conservative treatment. It is necessary first to evacuate the colon and rectum completely by regular bowel washouts over a period of three to six weeks, and then to purge and train the child to normal bowel habits.

Pathology.—In performing the preliminary colostomy in 10 cases recently, I have studied carefully the transition site between the dilated hypertrophied sigmoid and the more normal-looking rectum and rectosigmoid. The former suddenly narrows down to join the rather thin-walled flabby rectosigmoid which to the naked eye appears quite normal. The length of the normal-looking rectosigmoid varies considerably.

The histology of the dilated portion of the bowel showed hypertrophy of the muscle coats with normal distribution of the ganglion cells in the Auerbach's plexus. In the rectum and distal colon in two post-mortem cases and one specimen removed at operation studied by Dr. Martin Bodian at the Hospital for Sick Children, Great Ormond Street, the ganglion cells in the plexus of Auerbach were completely lacking. It is assumed that this defect seriously interferes with peristaltic movements of the affected bowel segment, and that this leads to secondary hypertrophy and dilatation of the intestine proximal to it.

Treatment of true Hirschsprung's disease.—With attention now focused on the rectum and rectosigmoid the surgical approach lies in the elimination of this portion of the gut as opposed to procedures directed towards the dilated hypertrophied portion.

Operation.—At the present moment there are in progress at The Hospital for Sick Children, Great Ormond Street, two-stage procedures for the removal of the rectum and rectosigmoid segments with preservation of the sphincters in 10 cases. Orvar Swenson in Boston (personal communication) is doing at the present time a pull-through operation with satisfactory cures.

Sympathectomy may have a place in the surgery of this condition in those cases in whom previous surgical procedures have rendered the new approach impracticable or perhaps in those cases in whom the abnormal spasmodic segment is very short.

CASE HISTORIES OF HIRSCHSPRUNG'S DISEASE

CASE I.—P. S. (fig. 1), aged 4 years. Height 39½ in. Weight 34½ lb. This child has been constipated since birth.

Bowel history.—There was no anomaly of the anus at birth. The meconium was noted to come away later than usual. The motions have always been small in diameter. A foul offensive flatus has been constantly present. He strains in an effort to pass his motion but has no pain.

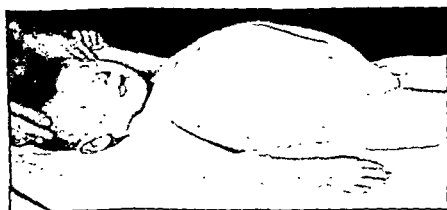


FIG. 1.—P. S., aged 4 years. Hirschsprung's disease showing abdominal distension and peristaltic wave in the sigmoid colon. Previous treatment includes three spinal anæsthetics.

Abdominal distensions.—This was noted to be severe at about 4 months of age. Sometimes the abdomen was very hard and tense, and at other times it was flat and deflated. His mother can deflate him either by abdominal massage or by the insertion of a high rectal tube.

Past history and family history.—Nothing relevant.

Present examination.—Sphincter normal tone, no faeces in rectum; rectum appears normal.

Investigation.—Barium screening shows normal-sized rectum; narrow spasmodic "trickle through" at rectosigmoid region, and a dilated colon above. Evacuation of barium was incomplete.

Treatment.—Liquid paraffin, abdominal massage, deflation with a rectal tube. Mechloly-bromide

X-ray examination.—In true Hirschsprung's disease rectosigmoid spasm or narrowing can always be demonstrated on the X-ray screen in the course of the barium enema and also in most cases on the film. The rectum is found to be of normal size, and the sigmoid above the rectosigmoid segment is dilated, and between the two a barium "trickle through" can be demonstrated on the screen and usually on the film. Evacuation of the barium is incomplete.

In the newborn baby the dilatation above the area of spasm may be absent or so slight in degree that the diagnosis remains in doubt, until the child is a few weeks old. In one baby an area of spasm was demonstrated in the rectosigmoid and sigmoid region, though no dilatation above has been visualized as yet.

In the cases of chronic constipation with faecal retention, after the bowel has been thoroughly evacuated of its contents, examination with the barium enema may show: (1) A long sigmoid loop of slightly increased but uniform diameter which extends distally to the rectum and anus with no evidence of persistent spasm. Evacuation of the barium is quite good; or (2) a terminal reservoir which fills with barium and extends from the anus through the distended rectum to involve the distal portion of the sigmoid. I have called this for descriptive purposes a terminal reservoir. There is no evidence of spasm and it evacuates the barium fairly efficiently.

In regard to the X-ray examination we have used with success a paraffin emulsion of barium which has the advantage of being more easily removed by bowel washouts from the sigmoid in true Hirschsprung's disease. The emulsion needs to be freshly prepared and used within a week:

Barium sulph.	5 oz.
Muc. trag.	2½ oz.
Glycerin	½ fl. oz.
Paraffin emulsion (50% liq. paraffin)	2 fl. oz.
Aq. ad one pint.					

In examining the rectosigmoid region with barium in Hirschsprung's disease it is necessary to allow only a very small quantity of barium to flow in under low pressure as the barium quickly passes through the small rectum into the dilated sigmoid and obscures the picture. Anteroposterior and lateral films are necessary at this stage in order to demonstrate this region properly.

Course of true Hirschsprung's disease.—In this series of cases the course of true Hirschsprung's disease has been one of recurrent obstruction relieved by flatus tubes, bowel washouts or a colostomy. Death has occurred in 10 out of 30 cases, and in the remainder various operations have been performed including spinal anaesthesia, sympathectomy of various types and partial and complete colectomy. None of these cases can be considered a cure, and the following five cases illustrating these procedures show evidence of persisting obstruction (*see* Cases I-V and Table I).

Type of treatment	Number of cases	TABLE I	
		Immediate	Late
Spinal anaesthetic (1-7 given)	22	In some peristalsis and evacuation of flatus were noted	Relapsed to previous state
Sympathectomy ..	3	1 improved for 3 years 1 no immediate effect 1 no effect	Relapsed to previous state Can now manage but still troubled with foul flatus, recurrent abdominal distension. Bowel dilated No effect
Colostomy-sigmoid ..	5	4 colostomy functions normally. General health greatly improved 1 dead	3 relapsed on closure 1 resisted closure and in good health with faecal fistula
Colostomy-transverse (preliminary to rectosigmoidectomy)	11	All function normally and are greatly improved in health	
Colopexy	2	? improvement	Relapsed
Sigmoid colectomy ..	1		Relapsed
Hemicolectomy ..	1		Relapsed
Total colectomy ..	2	1 improved 1 dead	Improved but gross distension of the ileum has occurred

CASE IV.—G. B. (figs. 5 and 6), aged $4\frac{1}{2}$ years. Weight $35\frac{1}{2}$ lb. Height 3 ft. 4 in. This child developed vomiting, constipation and abdominal distension four weeks after birth.



FIG. 5.—G. B., aged $4\frac{1}{2}$ years. Hirschsprung's disease. Showing dilated sigmoid and narrow rectosigmoid before partial colectomy.



FIG. 6.—G. B. Showing dilated transverse colon and narrow rectosigmoid after excision of left half of colon and anastomosis of the right half of the transverse colon to rectosigmoid.

Bowel history.—There was no anomaly of the anus at birth, and the meconium was passed at the usual time. When first seen at the age of 1 month the abdomen was distended with gas, and ladder patterns were visible. Constipation and gaseous distension of the abdomen have persisted.

Rectal examination.—At 4 weeks of age a suggestion of an inner sphincter was palpable at the tip of the finger.

There are no relevant details in the family or birth histories.

Treatment.—Bowel washouts have always been essential to relieve flatus and to evacuate the bowel. At the age of 2 years, an emergency transverse colostomy was performed. At the age of 3 years a partial colectomy was performed, the left half of the transverse colon, the descending colon and the sigmoid being excised. The right half of the transverse colon was anastomosed to the rectosigmoid segment using the spur technique, and the colostomy was finally closed at the age of $3\frac{1}{2}$ years.

Course.—Abdominal distension with peristaltic patterns, flatus and severe constipation have recurred.

Investigation.—X-rays show the narrowing of the rectosigmoid before the colectomy and afterwards, and the dilatation is now gross in the transverse colon proximal to the anastomosis.

CASE V.—M. G. (figs. 7 and 8), aged 15 years. Height 5 ft. 1 in. Weight $94\frac{1}{2}$ lb. This boy has had constipation since birth.

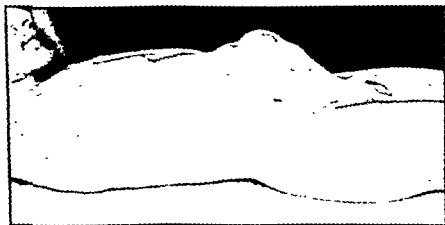


FIG. 7.—M. G., aged 15 years. Hirschsprung's disease. Recurrence of abdominal distension with peristaltic patterns after total colectomy.

FIG. 8.—M. G. Retouched X-ray to show relative diameters of terminal ileum and rectosigmoid segment.



FIG. 8.

and syntropan have been tried without success. At times regular enemas have been necessary. Three spinal anæsthetics have been administered without improvement.

Present situation.—Continual recurrence of abdominal distension associated with listlessness; constipation very persistent. Much foul flatus. General physique poor.

CASE II.—G. J. (figs. 2 and 3), aged 2 years 2 months. Weight 26 lb. Height 34 in. This child has been constipated since birth.

Bowel history.—There was no anomaly of the anus at birth. The meconium was noticed to be passed later than normal. Motions have always been small pellets. The child strains to pass his



FIG. 2.—G. J., aged 2 years and 2 months. Hirschsprung's disease showing abdominal distension.



FIG. 3.—G. J. Showing absence of distension after transverse colostomy which functions normally.

motion but there is no pain on defecation. The constipation has gradually increased and for the last six months has required enemas twice weekly in addition to liquid paraffin and medicines.

Abdominal distension.—This was first noted soon after birth. It is somewhat relieved by the passage of offensive flatus. Visible peristalsis has been observed.

Family history.—Nothing relevant.

Present examination.—Abdomen distended and tympanitic. The distension is central and in the flanks. Visible peristalsis and patterns noted. Ribs flared, umbilicus everted, no masses palpable.

Rectal examination.—Rectum empty, sphincter normal, upper end of the rectum appears to grip the tip of the finger.

Treatment.—Regular bowel washouts and medicines. Two spinal anæsthetics have been administered without alleviation of symptoms. A transverse colostomy was performed at the age of 2 years and 3 months. The subsequent course has been satisfactory with subsidence of distension, regular bowel actions from the colostomy and improvement in health.

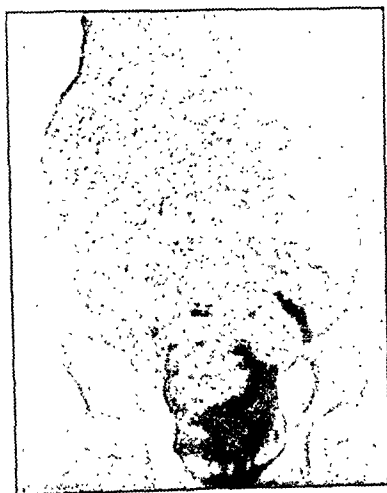


FIG. 4.—R. G., aged 9 years 8 months. Hirschsprung's disease showing persistence of dilatation of sigmoid after sympathectomy.

CASE III.—R. G. (fig. 4), aged 9 years 8 months. Height 4 ft. Weight 54½ lb. This child has been constipated since birth.

Bowel history.—There was no abnormality of the anus noted at birth. The motions have always been thin ribands or small pellets and accompanied by much flatus. He strains to defæcate but has no pain other than the ache caused by the abdominal distension. A number of medicines such as senna, milk of magnesia, syrup of figs, paraffin, &c., have been used without permanent relief. For the first two years he required daily enemas.

Abdominal distension was noted soon after birth.

Family history.—This child is one of twins (his twin brother is alive and well and is a much stronger and taller boy).

X-ray.—A barium enema reveals a distended sigmoid colon, a normal-sized rectum, but the rectosigmoid segment is small in comparison with the huge size of the sigmoid.

Treatment.—Medicines, four spinal anæsthetics, and a lumbar sympathectomy caused no noticeable improvement. Spasm, in the rectosigmoid segment, however, cannot now be demonstrated on the X-ray screen.

Present situation.—This child is listless, has recurrent attacks of abdominal distension and his constipation requires only an occasional bowel washout, but his bowels require constant care and attention. Foul flatus is a continual embarrassment.

Section of Urology

President—WALTER W. GALBRAITH, M.B., F.R.F.P.S.

[June 24, 1948]

DISCUSSION ON THE SURGERY OF URETHRAL STRICTURE

Mr. H. L. Attwater: The extreme gradualness of onset and the frequently insidious nature of its development place urethral stricture in an almost unique class. The initial cause is sometimes a trivial bacterial, chemical, or traumatic event; perhaps long forgotten before the actual contraction makes itself evident. Stricture is less severe to-day than formerly, no doubt due to the greater respect now paid to the canal during manipulations; the control of infection by penicillin and the sulphonamides has doubtless also led to further improvement.

Its slow onset is revealed by the fact that only 5% of cases appear in five years after the initial lesion, whilst some 66% become apparent in fifteen years or more, the average period of generation being 21.5 years (Beard and Goodyear, 1948).

One treatment, though not ideal, has stood the test of time. For some 3,000 years man has dealt with his strictures by means of dilatation but the necessity for extreme gentleness and patience in its use has only been appreciated comparatively recently (Attwater, 1943). From time to time attempts have been made to shorten the tedium of the process and, as early as the first century B.C., it would appear, from the nature of certain instruments discovered in parts of the Roman Empire, some form of external urethrotomy was practised; but even to-day no form of treatment provides a certain cure. All operations involving the urethra are in themselves traumatic procedures, and may be the precursors of stricture, so that there is every need for constant watchfulness and regular dilatations after them: "Once a stricture always a stricture."

SURGERY

The indications for surgical interference are: certain acute complications, a failure to achieve a reasonable result by means of dilatation, or, in some cases, to pave the way for more efficient dilatation later. Cases may fail to dilate because response to the stretching does not follow the usual progressive course. A stricture may be so dense that little, if any, advance can be achieved by the routine use of bougies or sounds; or frequent acute outbreaks of sepsis may make the attainment of even moderate relief impossible. Surgical interference may also be necessary in the case of irritable strictures, which are followed after stretching by fevers, rigors, or attacks of epididymitis. Calculi in the upper urinary tract or behind the stricture, or the spread of sepsis generally, may also demand it. Again, patients sometimes fail to stand up to the routine of dilatation; the fear of pain, and exaggerated sensitiveness, making them intolerant of the passage of instruments through a difficult stricture. In my experience the so-called resilient stricture is by no means a common variety and is often a type of irritable stricture, the apparent rapid return of the stenosis after dilatation being due to muscular spasm rather than to a quick reformation of the actual fibrous constriction. Such can often be circumvented by means of extreme patience and gentleness, or by the use of continuous dilatation by means of an indwelling catheter.

Impassable and impermeable strictures must be dealt with by some form of operative technique in order to gain control of the canal and enable the stenosis to be dealt with by appropriate measures.

URGENT SURGERY

In uncomplicated cases the onset of urgent symptoms, such as retention of urine, may require immediate operation. If the case is already known to have a constriction the state of the renal function may be already known, but in many instances the attack of retention occurs as a primary event. If, after the trial of all conservative measures, it is found impossible to pass any instrument *per urethram*, it is best to do a preliminary cystotomy and to drain the bladder. Special care is necessary if the renal function is low, and prolonged manipulations should be avoided (Stern, 1919). A patient with a chronically distended bladder due to stricture is in much the same position as a man with an enlarged prostate but, possibly because he is often in a lower age-group, he may stand more manipulation than the comparable case of prostatic enlargement. However, if such a case of retention reveals any symptoms of uræmia a rapid survey of the renal function should be made, and great care exercised, if the kidneys are badly compromised.

Urgent sepsis, such as the presence of extensive peri-urethral abscesses, or extravasation, DEC.—UROL. I

Bowel history.—There was no anomaly of the anus at birth. It is not known by the mother how long after birth the meconium was passed. From the first two weeks of life bowel washouts were necessary. The motion if passed spontaneously was like a thin riband of tooth paste in shape. At 3 months it was necessary to perform a colostomy because of a "stricture" three inches above the anus.

Abdominal distension.—The abdominal distension was noted at birth, and this was relieved by the passage of offensive flatus.

Past history and family history.—Nothing relevant.

Treatment.—The colostomy functioned satisfactorily and the child thrived. The colostomy was finally closed at 7 years of age, but the abdominal distension and constipation recurred. Between the years of 7 and 12 he required routine bowel washouts and rectal dilatation at regular intervals. At the age of 12 years, increasing abdominal distension, abdominal pain and vomiting necessitated further treatment in hospital. A barium enema X-ray examination revealed a rectosigmoid narrowing with enormous distension of the colon above this site. A total colectomy was performed in two stages, first a side-to-side ileosigmoidostomy, and later removal of the colon. At the first operation the rectum and rectosigmoid appeared normal and the colon was greatly dilated. The small bowel was not distended. Two months later abdominal distension with visible peristalsis recurred and further laparotomy did not reveal the cause of the obstruction.

Present situation.—Now 15 years old. The patient still suffers from some abdominal distension and much foul flatus, but with a carefully controlled diet in which he avoids the foods which cause him discomfort he can evacuate his semisolid faeces spontaneously.

On examination.—Much scarred abdomen, abdominal distension with visible peristalsis, audible borborygmi.

Rectal examination.—Some solid faeces in the rectum, sphincter normal, no narrowing palpable.

A barium X-ray now reveals a grossly distended ileum and a moderately large rectum but the upper rectum and remaining rectosigmoid appear of normal calibre with very sharp transition to the dilated ileum.

I wish to express my thanks to the surgeons and physicians of The Hospital for Sick Children, Great Ormond Street, for permission to use their cases in this work, to Dr. Benjamin Ward for his co-operation in the interpretation of the X-rays of these patients, and to Mr. Derek Martin for the photographic illustrations. My thanks are due also to Mr. Harold Edwards, for his kindness in providing me with Case V in this series.

DEMONSTRATIONS OF PATHOLOGICAL SPECIMENS BY RONALD W. RAVEN, O.B.E., F.R.C.S.

(1) Right hemicolectomy.

(a) Sarcoïd of ascending colon.

(b) Carcinoma of ascending colon.

(c) Chronic pyogenic infection of the ileocaecal region.

(2) Partial hepatectomy.

(a) Right lobe.

(b) Left lobe.

(3) Sacrococcygeal chordoma with microscopic preparations.

DRAWINGS.—Mr. Raven showed a series of drawings of sacrococcygeal cysts and tumours with reference to the embryology of the anorectal region.

OPERATIONS PERFORMED BY A. LAWRENCE ABEL, F.R.C.S.

for (a) Abdominoperineal excision of rectum.

(b) Hæmorrhoidectomy.

(c) Anal fissure, in the operating theatres, concluded the Meeting.

A new type of traumatic stricture, which illustrates the need for careful handling of the canal, has presented itself in this region in recent years, occurring after endoscopic resection of the prostate, the slight bruising caused during this procedure being capable of initiating a contraction. This is supported by the observations of Stratte and Stratte (1947) who have made a count of the separate movements of the resectoscope and cold punch in the hands of expert resectionists in the U.S.A. during prostatic resection. He finds that these average some 800 odd during resection and 150 or so more during the cold punch operation.

Chronic prostatitis and prostatectomy can set up a fibrous contraction of the internal meatus with occasional involvement of the prostatic urethra. The latter condition can often be extremely difficult to deal with, continuous dilatation followed by intermittent stretching being the method most frequently adopted, though perhaps the recent retropubic approach to the region may inspire some hope that this part of the canal may be attacked more directly in the future. Narrowing, if confined to the internal meatus, may be dealt with successfully, either by suprapubic cystotomy and the resection of a wedge from the neck, or by endoscopic resection of the constricting band.

There is little to be said here about the surgery of stricture of the urethra in the female, though these lesions are more common than is generally supposed (Daniel, 1939). They can be easily missed and may be the only lesions responsible for the patient's symptoms. They should not be neglected because, as the female urethra corresponds to the posterior canal in the male, and as the effect of a stricture varies inversely with its distance from the bladder, any contraction in the female canal will have, other things being equal, a more profound effect than the usual anterior stricture in man. Their ætiology is the same as in the male, but parturition must be added to the list of traumatic causes of injuries to the urethra. Most of the strictures are situated in the outer third of the passage (Pugh, 1932). The existence of congenital stricture in the woman has been denied but this is disproved by the fact that cases are on record which have existed from birth without evidence or history of injury or inflammation (Boyd, 1929a). Whilst the inflammatory varieties can be dilated the congenital stricture, whether a simple constriction of the external meatus, or taking the form of a little flap-like formation of the lower lip, can be readily dealt with by simple section.

CONGENITAL STRICTURES

A detailed description of the various congenital contractions of the urethra would be too long to include in the present discussion. In addition to pin-hole meatus other conditions of a highly diverse character are occasionally met with and may be situated in almost any part of the canal, sometimes affecting the urethra alone, and at others being only a portion of a widespread collection of deformities of the urogenital and other systems. Each case may present individual characteristics which may demand special methods according to the particular problem involved. They may present great difficulties during the course of surgical intervention and are often more fitted to the craft of the plastic surgeon than to that of the urologist.

SURGICAL METHODS

If dilatation of a stricture is inapplicable some method of surgical approach must be selected. Caulk (1931) has stated that, out of 45 cases dealt with by simple section, 2 were done by internal urethrotomy, and 43 by the external method, and that of uncomplicated cases only 0.6% to 1% were so dealt with. It must always be remembered that it only needs slight trauma to initiate a stenosis, and that it may take many years before the constriction becomes apparent. Any external or internal wounding of the urethra, therefore, may be followed by a contraction; and this would seem to be more liable to occur when the wounded area is the seat of an inflammatory fibrosis. Sepsis undoubtedly plays a part, both in the original genesis, and in the reformation of a stricture; and, although this may be modified by modern methods of control, the danger exists. For this reason it has always appeared to me to be better to deal with a case presenting urgent and complicating symptoms, not otherwise remediable, by a preliminary suprapubic and by subsequent dilatation when possible, rather than by cutting the stricture and adding trauma to sepsis.

A suprapubic allows inspection of both extremities of the blocked canal and will often permit dilatation to proceed as soon as oedema and spasm have subsided. Subsequent stretching also can often be carried out more easily and smoothly owing to the passage being at rest (King and Smith, 1935). If stretching is impossible urinary diversion provides a period during which sepsis can be controlled and will pave the way for a more deliberate approach later. Also during this time fistulæ in the neighbourhood of the stenosis which may occasionally refuse to heal and which are maintaining active sepsis can be dealt with by dissecting them out, and any other complication can be attended to before proceeding to the attack on the stenosis.

must be dealt with by urinary diversion, and appropriate incisions for the local drainage, according to the particular nature of the case. Antibacterial therapy, penicillin and the sulphonamides, should also be freely employed.

Traumatic lesions of the urethra with a view to preventing stricture must receive careful attention. Such cases fall into three classes: those which are due to actual wounding by flying fragments, stabs, &c.; bruises ranging from slight contusions to actual laceration, such as may result from kicks, falling astride beams and the like, which are usually situated in the bulbar area; and lastly major accidents such as the result of crushing injuries with fractures of the pelvis.

In the latter type, in which the urethra may be merely bruised, lacerated, or even torn completely across, the profound shock must first be combated. If the urethra appears to be damaged, in order to relieve retention a simple, not too determined, attempt to pass a small, soft rubber catheter is permissible, provided that efforts are not pursued too long or too energetically. If the catheter slips into the bladder, well and good but, if not, a suprapubic cystotomy should be done at once and the urine diverted. At the same time an incision may be made over any swollen area to evacuate blood-clot, or to drain an extravasation, and even in a suitable case to repair the torn urethra. This last, however, will often have to be deferred because of the shocked state of the patient, a careful watch being kept meanwhile for signs of extravasation or of pus formation.

As soon as permissible a careful investigation of the exact urethral deformity must be undertaken by means of cysto-urethrography, urethroscopy, or by sounding. If discontinuities are found, and the case allows the passage of instruments, gentle intermittent dilatation should be commenced. If, however, this is difficult or impossible, a careful exploration of the injured region by way of the perineum will be required, as soon as all evidence of acute sepsis has completely subsided.

There is one serious type of injury where, occasionally, as the result of a crushed pelvis, there is a complete division of the prostatic urethra and perhaps a wide separation of the segments by a collection of blood. An immediate suprapubic cystotomy and an opening up of the blood-filled cavity must be provided and, as soon as the condition of the patient will permit, an attempt should be made to approximate the severed portions of the urethra. If this is not done, either a complete block, or a severe form of stricture in the pelvic urethra, is certain.

Many traumatic urethral injuries are difficult to assess, and whilst it is easy to undertake too much, it is equally possible to be too conservative. Vigorous instrumental attempts to relieve retention, or to reach an exact diagnosis immediately after the injury by means of catheters, sounds, urethrosopes, or by the injections of radiopaque substances *per urethram* must be sternly held in check, and nothing but a simple gentle trial with a soft rubber catheter permitted. All such active measures may cause further laceration and spread infection; and even evidence derived by the use of a catheter may prove fallacious, unless carefully checked, as it may tap a pool of extravasated blood-stained urine which is not in the bladder at all, a condition, which if not appreciated, may lead to disastrous consequences.

Intravenous pyelography, which is reasonably safe in such cases, will sometimes reveal the nature of the injuries when the distribution of the shadows produced after the contrast medium has collected in the bladder is carefully studied (Boyd, 1929b; Troell, 1945).

DELIBERATE SURGERY

When surgical intervention in stricture is to be undertaken for any reason some form of deliberate approach must be adopted according to the requirements of the particular case; and the best results are to be expected when all septic reactions are completely under control. Any operation should cause the least possible trauma to the urethra because, although it may result in an immediate opening up of the canal, it may cause injurious stimulation to the constricting process already present. Any injury, however trivial, may cause stenosis, and wounding of the urethra, even when carefully performed during an operation, may result in subsequent contraction. For this reason, the simple cutting of a stricture, whether by internal or by external urethrotomy, cannot be regarded as certainly curative but only as a means of circumventing an awkward corner. Many cases no doubt cease to contract after cutting but such a result is fortuitous and should not be too optimistically anticipated.

About 70% of stenoses are situated a centimetre or so beyond the distal end of the membranous urethra in the bulb and from time to time all varieties occur in this locality, inflammatory, traumatic, and congenital; the impassable and impermeable types of these being the conditions which most often call for surgical interference. Such strictures are usually single in number though double or even multiple constrictions occur.

method is especially suitable for cases in which the narrowing consists of a single constriction in the perineal urethra.

The technique which I employ can be best illustrated by a short résumé of a case, the details of which have been already published. After a motor accident, which had caused a rupture of the bulbar urethra, an external urethrotomy had been done. This was followed by a tight stricture with a permanent perineal fistula. When I first saw him, five weeks later, there was an impassable stricture and all the urine was being passed by way of the fistula though fortunately the external sphincter was undamaged and he had a good control. There was a large tender mass in the perineum consisting of septic infiltration round the fistula and the site of the damage to the canal. A suprapubic cystotomy was done and nothing further was attempted for three months. By this time the perineal mass had greatly diminished in size though there was still considerable induration. The perineum was opened; all the indurated tissue was cut away by sharp dissection; and the two ends of the urethra were mobilized as far as I felt justified in doing so, and mobilization can be carried out extensively without fear of necrosis because of the good vascularity. In spite of this a gap of about 2 cm. remained even after tension sutures had been inserted in the posterior part of the wound. Accordingly a catheter was passed through the length of the canal bridging the raw gap, and the wound was lightly closed. Subsequent progress was uninterrupted and both suprapubic and perineal wounds were soundly healed in five weeks with a perfect functional result. Intermittent dilatation followed. (Attwater and Preiskel, 1933.)

This type of single constriction in the bulb will nearly always respond to such a method with a high proportion of good results and with modern uses of chemotherapy would seem to have a much wider application than formerly even when the urethral gap is complete and extensive.

If the ends of the urethra can be approximated without tension they should be accurately sutured. MacGowan (1923) does this by dividing the end of each segment longitudinally for half an inch (1.25 cm.) or so, so as to provide three flaps, or tags, one posterior, and two lateral ones, one on each side. The corresponding ends of these flaps are sutured together transversely, and the resulting longitudinal slits are either lightly sutured or left open. If the stricture can be excised together with all indurated tissue without completely sacrificing the mucosa at the site of contraction, this should be done whenever possible; a strip along the roof is usually retained to act as a bridge to encourage the proliferation of the epithelium.

When fibrosis has encroached upon the membranous and prostatic urethra, the outlook is often unfavourable and opinions as to the best method of dealing with them are divided. Excision of as much as possible and dilatation of the rest has been adopted by some. Others on a few occasions have attempted an elaborate deep dissection of the stenosed area by the Young (1936) perineal route through an inverted Y- or U-shaped incision, but during all such proceedings great care must be taken to avoid injuring the external sphincter or its nerve supply which may result in an uncontrollable incontinence.

Actual plastic proceedings in cases of excision of the bulbar urethra are rarely called for, but if, owing to massive destruction of the canal, no sort of approximation can be made, a skin flap can be grafted across the whole deficiency between the two openings of the severed urethra, thus converting the gap between the widely separated segments into a temporary skin-lined gutter with the anterior extremity of the membranous and prostatic urethra opening on to it behind and the posterior end of the anterior segment leaving it at its distal extremity. As soon as this flap has safely healed further procedure involves the refashioning of an intervening channel which will fill the space between the two urethral openings. This is done by means of two lateral flaps turned inwards so as to reform the canal lined with skin connecting the segments of the urethra. The resulting raw area is in turn covered by a graft. Such procedures are akin to those used in some cases of hypospadias when using the Ombredanne technique.

As a rule, however, in the absence of inflammation and sepsis, reliance can be placed on the natural tendency of the urethral mucosa to proliferate quickly and to cover a raw gap, which may have been left after an excision, even when this is of an extensive nature.

In recent years some attempts have been made to make more certain of a rapid epithelial regeneration by passing a catheter when the excision is completed, a skin graft being wrapped round the catheter with the epithelial side inwards. The instrument is so adjusted that its graft-covered portion bridges the raw space in the canal, the essential being to bridge any part of the urethral channel which has been denuded of its mucosa with healthy epithelium as soon as possible.

I suggest, therefore, that in the treatment of stricture the method of intermittent dilatation, though not ideal, is still the method of choice; and that, if circumstances render surgery necessary, simple division of a contraction, either by internal or external urethrotomy, is not enough (it may be used on special occasions but is apt to be followed later by recontract-

EXTERNAL URETHROTOMY

That urethrotomy cures is a fallacy, it only provides an immediate relief, often temporary, to the most painful and dangerous symptoms, and in too many cases it is followed later by a recontraction perhaps in a worse form than before.

There are two ways of doing an external urethrotomy: (1) The Syme technique, in which a special narrow-ended grooved staff is passed and cut down upon. This demanding as it does the passing of an instrument through the stricture was never extensively practised because it did not deal with the impassable case and only complicated subsequent dilatations.

(2) When no instrument could be passed some form of Wheelhouse technique held the field for a long period and is still practised. Without going into operative details, which are well known, there is, however, a noteworthy point. In the past tracing the narrow stenosed part of the canal was often extremely difficult, even with the use of methylene-blue staining to facilitate the finding of the narrow path, or by a deep dissection of the perineum and opening the urethra behind the stricture, thus allowing the latter to be attacked both behind and in front.

This finding of the urethral lumen within the stricture has usually been regarded as obligatory but my colleague Loughnane (1941) cuts down on a sound in the anterior urethra and withdraws it with a 22F rubber tube threaded over its tip, thus implanting the tube in the anterior urethra from the perineal wound to the external meatus. He then passes a retrograde sound from the suprapubic opening and cuts down on its tip, where it bulges in the perineum. He now withdraws it with the perineal end of the rubber tube threaded upon it. This tube now passes continuously from the external meatus to the bladder and out through the suprapubic opening. It is fixed in position by a safety pin at either end. No notice is taken of the constricted part of the canal which is by-passed. If there is a fistula, or the perineal wound is septic, it is loosely packed with acriflavine gauze and allowed to granulate. The rubber tube is rocked to and fro daily, and changed weekly for a larger size, until 30F is reached. It is retained until the perineal wound is healed. A 28/32 Clutton sound is then passed intermittently at increasing intervals until a space of six months is attained which is kept up indefinitely.

INTERNAL URETHROTOMY

I have always regarded internal urethrotomy as having a limited application. It presents a dangerous appeal because it cuts short the distresses and difficulties of urethral stricture in an almost dramatic manner and is, therefore, pleasing to both patient and operator alike. Unfortunately far too often it fails to produce a lasting result, and the subsequent recontraction is frequently so hard as to be quite undilatable, demanding a second application of the urethrotome, or even more extensive interference. Moreover, the proceeding itself is not free from danger and may be followed by untoward symptoms from bleeding and sepsis.

There are, however, a few occasions when the method may be useful. When for some reason it is necessary to obtain a quick restoration of the urethra to an approximate normal (Lowsley, 1935); when after a previous internal urethrotomy a stricture has become so indurated and gristly as to be quite undilatable (Lazarus, 1941); or it may be used sometimes when dealing with a true resilient stricture though this type is not so common as is sometimes imagined; and lastly strictures have been so dealt with on occasions as a preliminary to an urgent cystoscopy or lithotripsy, or when the patient finds it impossible to attend regularly for treatment of a narrow stenosis.

As this operation seems to be an apparent short cut to normality it is popular with military surgeons because of its comparative simplicity and frequent good immediate results, permitting the man to be returned early to duty (Botsford, Harrison and Trichel, 1945). It is forgotten, however, that a traumatic stricture may have been superimposed upon an inflammatory one or that a later recurrence of the contraction may be much worse than the original.

EXCISION

If the stricture-bearing area can be wholly removed, the edges of the divided urethra accurately joined, and if healing takes place with a minimum of scar formation, excision holds out a far greater hope of permanent relief than any other method; but again, owing to the slow and insidious onset of recontraction, it would be a bold man who with present knowledge would give his patient *carte blanche* as being completely cured, even after excision. The only safe course is to maintain careful supervision and six-monthly dilatations.

The first urethral excision was done about the year 1812 but produced no results to encourage its being generally adopted and it was not until Legueu introduced preliminary suprapubic diversion of the urine that surgeons began to look upon excision with any favour. Drainage of the bladder permits the control of sepsis at the site of the stenosis and often renders the case suitable for the removal of the diseased portion of the canal. The

External urethrotomy is essential in some instances but it does lead to a greater amount of fibrosis afterwards. Marion's method of urethroplasty seems to me to be limited in its application to cases of traumatic stricture where only a short length has been affected by fibrosis; in strictures of inflammatory origin, the urethral narrowing usually spreads for a considerable distance beyond the grossly constricted portion of the urethra. I have carried out urethroplasty in half a dozen patients and I do not regard it as curative since they all required regular dilatation; one patient, after two easy dilatations, failed to report for two years when his stricture was found to have reformed and was so tight that an external urethrotomy had to be performed. Marion actually mentions in his book that he sometimes has to carry out an external urethrotomy after his operation to permit of the initial dilatation. I have been struck by the fact that sexual function is not impaired, and may be actually improved, following urethroplasty and three of my patients, at least, have had no trouble with intercourse.

One type of stricture will not respond to dilatation and that is the meatal. Where only the external meatus is involved a simple meatotomy will suffice but I have encountered a number of patients with extremely tight strictures of the meatus where the process has spread back until it involved the last 2-3 cm. or more of the urethra. Many of these people have shown, in addition, a peculiar induration of the glans and it was not possible to relieve them by the usual type of meatotomy. In such cases it is my practice to create an artificial hypospadias by making a short incision immediately behind the glans and then stitching the urethra, diamond fashion, to the skin. This gives a complete relief and does not interfere with sexual function. The urinary stream is apt to spray but this can be minimized if the incision used is short. I do not know what the ætiology of this peculiar condition is but, once started, it appears to be progressive and it may spread back for a considerable distance. After the creation of the artificial hypospadias the glans loses its induration and becomes soft and supple.

Mr. H. Hamilton Stewart: I wish to describe briefly a procedure which I have carried out for the treatment of cases of generally contracted and strictured penile urethræ. There are two essential prerequisites.

(1) The urethrogram should reveal that the urethra behind the region of the peno-scrotal angle is of normal calibre.

(2) A foreskin should be present.

Stage I.—Having discovered that the region of the bulb and posterior urethra are normal, the penile urethra and skin on the ventral surface of the organ are split down the middle line until the normal urethra is reached. The external urethral orifice is now situated in the region of the peno-scrotal angle or just behind it. The cut edge of the skin and mucous membrane of the urethra at the new external urethral orifice are sewn together with ten-day fine catgut. Elsewhere the skin and mucous membrane of the guttered urethra are sutured together with fine nylon sutures.

Stage II.—After a period of three months or longer a plastic operation of the Ombrédanne type is performed. A skin flap is obtained from the scrotum and the foreskin is also utilized.

Stage III.—This is carried out exactly as advised by Ombrédanne, and is a very important part of the operation. This stage should not be performed until at least two months have elapsed after the second stage.

This procedure makes it unnecessary for any further instrumentation to be carried out, and the organ erects in a perfectly normal manner.

I strongly recommend this procedure for the treatment of these difficult cases.

[Lantern slides of urethrograms before and after operation were shown.]

Mr. H. P. Winsbury-White: Mr. Attwater rightly called attention to the seriousness of stricture in the female. I have seen a number of these cases and I entirely agree with him. It has been my experience that when one of these cases comes to the Out-patient Department it is often impossible to get even a filiform bougie through the obstruction, and one generally has to admit the patient to hospital for treatment under an anæsthetic. Subsequently unremitting attention for dilatation is required.

These female patients are undoubtedly very prone to attacks of pyelonephritis.

With regard to treating an impermeable stricture by the retrograde method, I have done several cases in this way and have found the ultimate results highly satisfactory. When suprapubic cystostomy is carried out for the relief of retention of urine in stricture cases if the drainage is continued indefinitely the stricture will get very much worse, and at last may become impermeable. It is therefore necessary to see that the suprapubic drainage is not unduly prolonged. On the other hand relief of the retention due to stricture by suprapubic drainage benefits the stricture when the drainage is continued only for a short time.

External urethrotomy in the ordinary sense is, in my experience, a very bad operation.

tion of the stenosis in a more intractable form than the original); and that, whenever possible, after diversion of the urine in order to gain control of all septic reaction in the field of operation, a complete excision of the stenosis together with all inflammatory induration should be adopted. During all such proceedings every effort must be made to avoid unnecessary trauma and the new canal should be afforded every opportunity of relining itself with healthy mucosa as quickly as possible.

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Mr. William S. Mack: There is a general impression that, with the advent of sulphonamides and penicillin, gonorrhœa and non-specific urethritis have ceased to give rise to urethral stricture. I am by no means convinced that this is so and I still encounter early strictures during routine urethroscopies on treated cases of gonorrhœa; these patients have all had previous attacks of urethritis, either gonococcal or otherwise, and the strictures are presumably caused by these previous infections. The ominous feature, however, is that some of these patients were treated in the past purely by sulphonamide and were dismissed "well" after a smooth and rapid recovery. Figures are fallacious but the following are of interest: During 1935 and 1936 just before sulphonamides were used in treatment, 3,142 male patients, suffering from acute gonorrhœa, were dealt with in the Corporation of Glasgow Venereal Diseases Clinics. During routine tests of cure, five patients of this series were found to have urethral stricture on urethroscopy. During 1946 and 1947, 18 examples of urethral stricture were detected on urethroscopy out of 6,082 patients with acute gonorrhœa. On questioning a number of these patients it was found that some of them had had their previous attack of gonorrhœa subsequent to 1936 and had been treated with one or other of the sulphonamides only; there was nothing in their story to suggest that progress had been slow.

These figures do not include cases of stricture found in patients with non-specific urethritis, since the record system in Glasgow does not deal with this, but there is no doubt that non-specific urethritis has increased greatly during recent years and that it is often difficult to clear up. Stricture can, and does, follow these non-specific infections of the urethra. While non-specific urethritis may represent a clinical entity, many patients suffering from it give a history of a previous gonorrhœa and there seems no doubt that some examples of the condition do represent the end-results of this antecedent infection. It is not uncommon, indeed, to find that a mild urethral discharge is due to a stricture and the discharge may be present for many years before there is any disturbance of micturition. Possibly the public is more "venereal disease conscious" as a result of so much propaganda and it may be that patients with very early strictures are going to venereal diseases clinics rather than waiting until they develop dysuria. I am convinced that gonorrhœa is still playing a major part in the ætiology of stricture in spite of modern methods of treatment. It is still too early to say what will happen with penicillin—after all, strictures do not cause dysuria for many years after they have begun to form—but it is well known that penicillin-treated gonorrhœa may leave a patient with a slight urethral discharge for months afterwards; it may be that this represents a mild inflammatory process which will later give rise to a stricture.

There are, as the opening speaker has pointed out, few advances in the actual treatment of stricture, and treatment depends largely on individual preferences. I prefer to rely on very slow and gentle dilatation and to avoid operation, unless this is absolutely necessary. Where operation is required I generally employ internal rather than external urethrotomy. The urethrotome merely divides the fibrous ring at one part and thus permits of dilatation.

Section of Odontology

President—HUMPHREY HUMPHREYS, O.B.E., M.C., M.B., F.D.S.

[May 24, 1948]

MEETING HELD AT THE ROYAL COLLEGE OF SURGEONS, LONDON

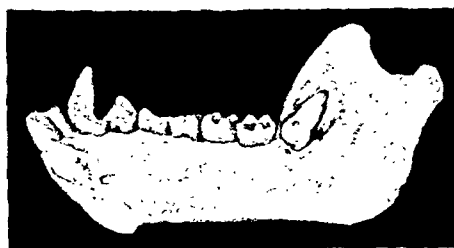
Variations of the Teeth of the Green Monkey in St. Kitts

By Sir FRANK COLYER, K.B.E., F.R.C.S.

THE Green Monkey (*Cercopithecus aethiops sabaeus*), whose normal habitat is West Africa, was introduced into the West Indian island of St. Kitts by the French when it was in their possession. I am informed by Mr. Carleton Evelyn that the monkey "has been locally established for quite 250 years. Père Labat who visited the island in 1700 speaks of some of them being shot and of others kept as pets, which indicates that they were then well established, and Dr. Graenger writing some years later calls them 'the pest of Liaminga's hills.' They are still a pest destroying the sugar cane, ground provisions and anything that they can lay hands on. The wild berries would appear to be the chief diet of those living in the high wooded area of the island."

In the early part of 1939 I received from Mr. Carleton Evelyn a parcel of 14 skulls and amongst them were two showing numerical variations. As it was possible that this marked rate of variability was a fortuitous circumstance I decided to try and obtain more material. Unfortunately war broke out and it was not until last year that further consignments of skulls were received, bringing the number available for investigation up to 92, a number sufficient to allow a fairly reliable idea to be gained of the variability of this animal.

The permanent dentition is present in 76 skulls and amongst these are four with numerical variations of the teeth. The details are as follows:



(i) Male. An extra tooth—unerupted—posterior to the mandibular right third molar. The tooth, as shown in fig. 1, is embedded in the ramus, the crown is close to the third molar and the root is directed upwards (A. 72.615).

FIG. 1.—*Cercopithecus aethiops sabaeus* (The Green Monkey). Right half of the mandible, view of the inner surface. An extra tooth is embedded in the bone posterior to the third molar. The bone has been removed to uncover the root of the tooth (A. 72.615).

(ii) Female. An extra incisor in the left side of the mandible (A. 72.63).

(iii) Female. An extra incisor in the left side of the mandible. In this specimen the mandibular right third molar and the right maxillary third molar are misplaced as shown in figs. 7 and 9. On the external aspect of the roots of the mandibular third molar there is a web of cement which extends about two-thirds down the roots. In each maxillary third molar the external roots are fused with the internal root (A. 72.6712).

(iv) Female. The mandibular right third molar is absent. The mandibular first molars are rotated, which is a rare positional variation (A. 72.637).

The number of skulls showing absence of, or extra teeth is 5.3%, which is a marked variability in a species. In 104 skulls of animals from Africa, some of which had been in captivity, there were two extra teeth, a percentage variation of 1.9.

Amongst the twelve skulls with the deciduous dentition in position there is one in which the crown of the mandibular right second incisor shows partial dichotomy (A. 72.6361).

Variations in the number of the roots of the third molars are present in 20.8% of the 72 skulls in which the teeth are fully, or almost fully, formed. The variations of the maxillary teeth are fusion of the external roots, of the postero-external and internal roots, of all three roots. The variations of the mandibular teeth are fusion of the anterior and posterior roots on their internal aspects and complete fusion of the roots. The variations are not always symmetrical; in one case of fusion of the postero-external and internal roots of the left maxillary tooth the right tooth is normal in shape, and in another of complete fusion of the roots of the maxillary third molar the right tooth alone is affected.

* The numbers refer to the catalogue of the Odontological Section of the Royal College of Surgeons' Museum.

The worst strictures I have seen are those which have been subjected to this method. On the other hand internal urethrotomy is a most excellent procedure in many cases. There are some cases, however, in which the operation is quite inadequate.

So far nobody has mentioned continuous dilatation as a treatment of stricture. This method I have found highly satisfactory in difficult out-patient cases where intermittent dilatation was found to be inadequate. The patient is admitted to hospital and successively increasing sizes of instruments are placed in position during the course of a few days. In this way a bad stricture can be dilated up to a fairly large calibre within a week with the least possible traumatism resulting.

Excision of the stricture I reserve for certain traumatic cases of the bulbous or penile urethra. This operation is satisfactory with these cases because the constriction tends to be more localized than is sometimes the case in the extensive stricture resulting from inflammatory and other causes.

Mr. A. Wilfrid Adams: Post-prostatectomy Obliteration of Penile Urethra.



FIG. 1.—Pre-scrotal meatus for post-prostatectomy stenosis of urethra.

A patient was sent to me with permanent suprapubic drainage which he had had for a year since removal of his prostate. He was aged 66, healthy in general appearance but somewhat resentful in expression.

On examining the penis the meatal margins were seen to be normal but the opening was sealed and smooth, suggesting congenital absence of urethra. I examined the proximal urethra via the suprapubic opening and found tight stenosis of the internal meatus through which a sound could be passed as far as the root of the penis. The whole shaft of the penis was impermeable.

He was anxious to dispense with the tube so I divided the urethra at the penoscrotal junction, exteriorized it there, dilated the neck of the bladder and the suprapubic fistula healed. He is more than grateful for the restoration of micturition which is perfectly free still.

The aetiology of this case is, presumably, traumatic urethritis from an indwelling catheter during his prostatectomy. The surgeon avers that the catheter was not in the urethra unusually long. Such perfect obliteration of the distal few inches of the urethra in this connexion is unique in my experience.

Mr. A. W. Badenoch: The retropublic approach is undoubtedly the best when dealing with rupture of the prostatic urethra seen soon after injury. When a stricture has been established, however, I have found it impossible to expose the urethra on account of scarring from dense fibrous tissue, and certainly, in my experience, this approach has not helped in the treatment of a fully developed stricture of the prostatic urethra. In a recent case, a man of 26 years had had an injury nine months previously. This was treated by suprapubic cystotomy, and in spite of subsequent operations there had been complete failure to pass an instrument along the urethra since the injury. I exposed the prostatic urethra but it was impossible to identify the stricture. The bulbous urethra was exposed in the perineum, the torn distal end identified, and the urethra freed for about one inch. A metal bougie was passed retrogradely and the stricture broken through. The open end of a catheter was attached to the bougie and brought into the bladder. The pointed end was passed retrogradely along the bulbous urethra, and the torn end of the latter was sutured to the catheter. The catheter was then pulled up into the bladder, bringing the bulbous urethra with it to lie in the region of the prostatic urethra. This catheter was kept in position as a splint for ten days, the bladder being drained suprapubically. On removal of the suprapubic tube at the end of fourteen days, the patient was able to pass water. A full-sized instrument can now be passed.

It is interesting to note that while the patient had been impotent for the nine months between his injury and this operation, his potency has now returned.

shown in fig. 3. The tooth, it will be observed, is situated in a more vertical position than in fig. 2, but the slight inward inclination is still present. A further movement upwards impels the crown of the tooth along the posterior surface of the second molar and brings it into a vertical position. These stages are shown in figs. 4 and 5. In fig. 4 the anterior border of the occlusal surface has reached the crown of the second molar, in fig. 5 the tooth has moved into a vertical position.

It seems, therefore, that if the tooth is to take its normal place in the arch the tooth-bud must be given off from the tooth-band in a position which, at a certain stage of growth, will bring the convex surface of the anterior aspect of the crown into the concavity in the posterior surface of the second molar.

The mandibles with misplaced third molars are as follows:

(i) In the one shown in fig. 6, the crown of the third molar is impacted against the root of the second molar. This abnormality is probably due to the tooth-bud being given off from the tooth-band with such a forward inclination that the occlusal surface tends to reach the root of the second molar lower down than the concavity at a stage when the growth of the roots is complete.

Here, I think, is a convenient place to refer to the difficulty in deciding whether a growing third molar is likely to move into a correct position or into one where it will be impacted against the second molar. As long as the roots are not fully formed there is always the possibility that the apparently tilted tooth may right itself, but where the root is fully formed and the crown is in contact with the root of the second molar well below the concavity then the probability is that the tooth will become impacted.

(ii) In the second mandible the third molar has erupted with the occlusal surface directed well inwards and the external surface so much upwards that in occlusion it is this surface and not the occlusal surface which comes in contact with the maxillary tooth. This abnormality may be traced to an undue tilt inwards of the developing tooth (A. 72.58).

(iii) The third mandible is shown in fig. 7. The tooth has erupted on the inner aspect of the bone with the crown directed inwards and forwards. This abnormality may be regarded as a marked example of the type of variation present in the second mandible. The tooth has moved in its developmental direction and has failed to contact the root of the second molar and so has not rotated into a vertical position.



FIG. 6.—*Cercopithecus aethiops sabæus* (The Green Monkey). Right half of the mandible. The third molar is unerupted and impacted (A. 72.647).

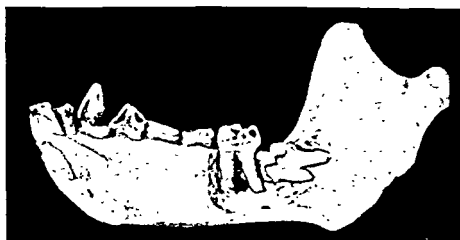


FIG. 7.—*Cercopithecus aethiops sabæus* (The Green Monkey). Right half of the mandible, view of the inner surface. The third molar has erupted on the inner aspect of the bone (A. 72.6712).

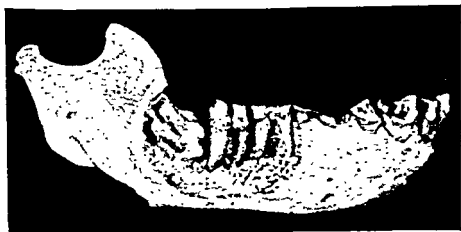


FIG. 8.—*Cercopithecus aethiops sabæus* (The Green Monkey). Right half of the mandible. The third molar is much misplaced (A. 72.671).

(iv) The fourth and most interesting case is in the mandible of an old female. On first examining this specimen I thought it was an example of a missing molar but just posterior to the second molar there was a small hole and at the base of this the crown of a tooth could be detected. On removing the bone the third molar was found to be in a horizontal position in the base of the ramus as shown in fig. 8. The crown is directed downwards, a little inwards and is rotated slightly, the lower part which is the normal anterior surface facing upwards. Considerable difficulty was encountered in removing the bone which in places was closely adherent to the tooth, unfortunately a small portion of the anterior root was cut away by the drill. A curious feature about

Fusion of the roots of the mandibular first molar, which is an uncommon variation in monkeys, is present in one specimen (A. 72.6713). Unfortunately investigations of the roots of teeth often involve damage to the specimens and as several formed parts of collections in other museums the number available for examination was limited. In the 36 skulls it was possible to examine there were three with fusion of the roots of the maxillary third molar or 8.3% of the specimens.

In addition to this marked rate of variability in number and shape of the teeth there is also a high rate of variability in the position of the teeth. An abnormal arrangement of the maxillary incisors is present in just over one-quarter of the skulls; the abnormality consists in the protrusion of one or both first incisors beyond the line of the second incisors. In 8 cases the abnormality is well defined.

Positional variations of canines are rare in the apes and monkeys, the variation when present being almost entirely confined to the mandibular teeth. In this series of the Green Monkey there is a mandible in which the right canine has moved in a backward direction and in occlusion impinges against the inner surface of the maxillary tooth which it has displaced outwards (A. 72.639).

In 16 of the skulls there are variations in position of the premolars, the abnormality taking the form, in most cases, of rotation or displacement inwards of the maxillary second premolar; in four of the specimens the abnormality is marked. By far the most interesting variations are those of the third molar. There are four cases of misplaced mandibular teeth and one of a misplaced maxillary tooth. Before, however, describing these most interesting variations it may be instructive to glance at the positions of the third molar in the bone during the period of growth as, I think, they shed light upon the development of the misplaced third molar.

At an early stage in the growth of the mandibular third molar, as shown in fig. 2, the crown of the tooth is tilted well forwards with a slight inclination inwards, the anterior border of the occlusal surface being close to the posterior root of the second molar. With the growth of the root the crown moves upwards and the convex surface of the anterior portion passes into the hollow in the posterior aspect of the second molar; this stage is

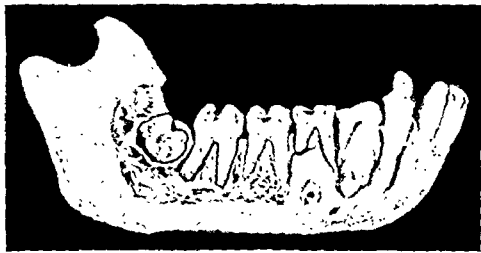


FIG. 2.—*Cercopithecus aethiops sabaeus* (The Green Monkey). Right half of the mandible. An early stage in the growth of the third molar. The anterior border of the occlusal surface is close to the posterior surface of the second molar (A. 72.61).

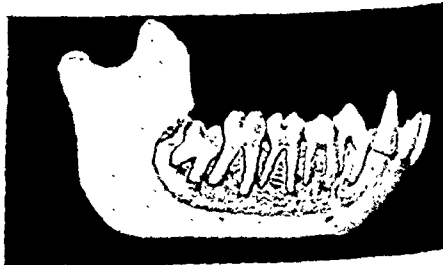


FIG. 3.—*Cercopithecus aethiops sabaeus* (The Green Monkey). Right half of the mandible. The convex surface of the anterior portion of the crown of the third molar has moved into the concavity in the posterior surface of the second molar (A. 72.614).



FIG. 4.—*Cercopithecus aethiops sabaeus* (The Green Monkey). Right half of the mandible. The anterior border of the occlusal surface of the third molar has reached the crown of the second molar (A. 72.651).



FIG. 5.—*Cercopithecus aethiops sabaeus* (The Green Monkey). Right half of the mandible. The third molar is fully erupted (A. 72.665).

shown in fig. 3. The tooth, it will be observed, is situated in a more vertical position than in fig. 2, but the slight inward inclination is still present. A further movement upwards impels the crown of the tooth along the posterior surface of the second molar and brings it into a vertical position. These stages are shown in figs. 4 and 5. In fig. 4 the anterior border of the occlusal surface has reached the crown of the second molar, in fig. 5 the tooth has moved into a vertical position.

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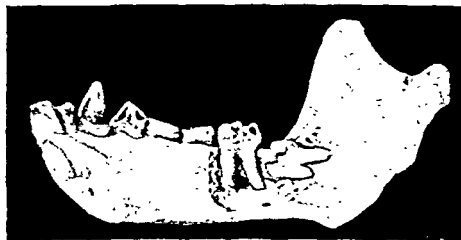


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FIG. 8.—*Cercopithecus aethiops sabæus* (The Green Monkey). Right half of the mandible. The third molar is much misplaced (A. 72.671).

(iv) The fourth and most interesting case is in the mandible of an old female. On first examining this specimen I thought it was an example of a missing molar but just posterior to the second molar there was a small hole and at the base of this the crown of a tooth could be detected. On removing the bone the third molar was found to be in a horizontal position in the base of the ramus as shown in fig. 8. The crown is directed downwards, a little inwards and is rotated slightly, the lower part which is the normal anterior surface facing upwards. Considerable difficulty was encountered in removing the bone which in places was closely adherent to the tooth, unfortunately a small portion of the anterior root was cut away by the drill. A curious feature about

the tooth is a linear gap about the junction of the crown with the root on the anterior aspect of the tooth. This line is discernible in the illustration and is clearly seen in the radiograph which was taken of the tooth. The exact nature of the defect cannot very well be ascertained without destroying the tooth but the radiograph seems to point to some absorption of the dentine.

A rare variation of the second molar is present in this mandible. Both teeth are rotated, the anterior surfaces having swung inwards and the posterior outwards. In the maxillæ the third molars have the crowns tilted backwards and the antero-external roots of the third molars are overlapped by the postero-external roots of the second molars. The right second molar is displaced slightly inwards and is in abnormal occlusion with the mandibular tooth. The antero-external and internal roots of the maxillary third molars are joined by a web of cement.

The growth and eruption of the maxillary third molar is similar to that of the mandibular tooth. At the stage before the crown is fully formed the tooth is high up in the tuberosity with the occlusal surface directed downwards and slightly forwards. With the formation of the roots the tooth moves downwards and passes into the concavity in the posterior surface of the second molar and then rotates and assumes a vertical position in the arch with ample room between its antero-external root and the postero-external root of the second molar.

Impactions and other abnormalities of the tooth are much less common than is the case with the mandibular tooth and this is probably attributable to the less resisting character of the bone of the tuberosity which allows the crown to move freely backwards. The occlusal surface, even when there is ample room in the arch, is often directed a little backwards with ample room between the roots of the second and third molars. Impaction of the

crown of the maxillary third molar against the root of the second molar does occur but the usual form of positional variation is an exaggerated backward inclination of the crown accompanied by a corresponding forward movement of the roots so that the antero-external root passes under the postero-external root of the second molar. This condition is present in two of the skulls. The most marked example of a misplaced maxillary third molar in the series is shown in fig. 9. The crown of the right tooth is tilted towards the palate and is in abnormal occlusion with the mandibular tooth.

Amongst the skulls of animals from West Africa there was only one showing positional variation of the third molar and in that specimen the mandibular right tooth was slightly inverted.

The facts related above show (i) a marked variability of the teeth of the Green Monkey in

St. Kitts, and (ii) that it is varying more than the animal in its normal habitat. It is of interest to speculate whether this increased variability is due to the altered environment of the animal.

There is evidence that positional variations may be related to variations in number and shape¹. Examples of the relationship are seen in *Erythrocebus* amongst the Old World Monkeys and *Cebus* and *Ateles* in the New World Monkeys. This series of Green Monkeys from St. Kitts is another example of the relationship and the marked variability in the number of roots of the third molars and the comparatively large number of misplaced third molars is most instructive.

¹See Colyer, F. "Variations and Diseases of the Teeth of Animals", London, p. 465.



FIG. 9.—*Cercopithecus aethiops sabæus* (The Green Monkey. (Cranium. The right third molar is misplaced (A. 72.6712).

Section of Orthopædics

President—GEORGE PERKINS, M.C., F.R.C.S.

[May 4, 1948]

Paget's Disease Commencing at the Age of 30.—DAVID LEVAY, M.S., F.R.C.S.

A woman of 37, complaining of *backache*, was found on radiographic examination to have collapse of the second lumbar vertebra (fig. 1).

Further investigation showed changes due to *Paget's disease* in the skull and left femur but in no other bones (figs. 2 and 3).



FIG. 1.

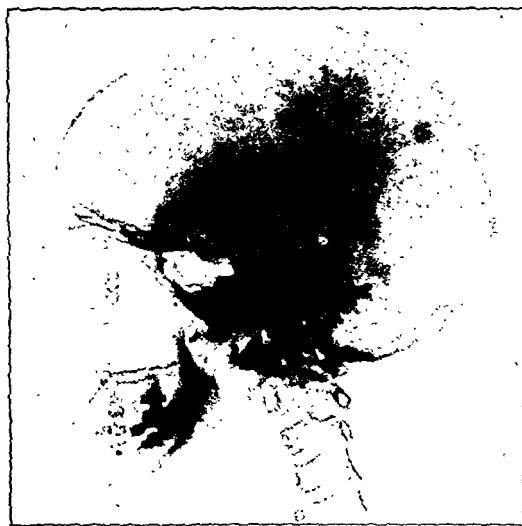


FIG. 2.

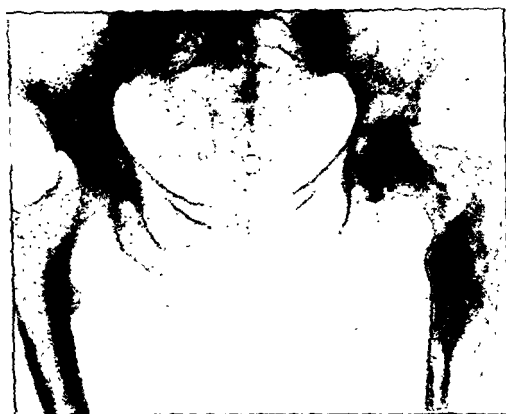


FIG. 3.



FIG. 4.

There was a history of a pathological fracture of the left femur at the age of 30, and recourse to the original radiographs showed a typical fracture due to *osteitis deformans* (fig. 4).

The patient's father and a paternal uncle both suffered from the disease.

DEC.—ORTHOP. I

Fracture-Dislocation of Cervical Spine.—DAVID LEVAY, M.S., F.R.C.S.

On 13.6.47 a woman of 42 sustained a fracture-dislocation of the fifth on sixth cervical vertebra, as the result of a heavy cupboard falling on her head at work (fig. 1).

There was quadriparesis, mainly affecting the right arm, and respiratory embarrassment. Skull traction was applied, and reduction completed by manipulation under pentothal anaesthesia after forty-eight hours.

On 4.7.47 wiring and grafting were performed, with post-operative immobilization in a leather collar, which was retained for twenty weeks.



FIG. 1.



FIG. 2.

The neck is now painless and fusion is sound, though the radiograph shows that consolidation has taken place in a position of slight forward subluxation (fig. 2). Function in the right arm has improved considerably, and the other limbs are normal. She is doing most of her own housework.

Congenital Bowing of the Tibia.—J. A. CHOLMELEY, F.R.C.S.

R. W., male, born 4.9.38.

History.—Forward bowing of left tibia was first noticed at 15 months old. There was no history of injury.

September 1941: Admitted to Hertford County Hospital where a wedge osteotomy of



FIG. 1 (13.6.41).—Condition on this date.

FIG. 2 (1.5.43).—Showing plate and non-union.

the left tibia and fibula was carried out. The tibial osteotomy was fixed by a plate (two screws broke after insertion).

February 1942: Walking plaster applied.

May 1942: Plaster removed.

June 1942: Walking plaster reapplied as there was no sound bony union.

September 1943: Plate removed. Clinically and radiologically ununited fracture of tibia below the site of osteotomy.

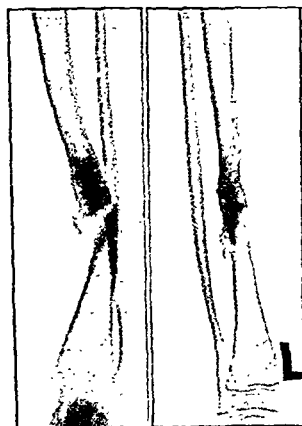


FIG. 3 (11.1.44).—Showing non-union after removal of plate.

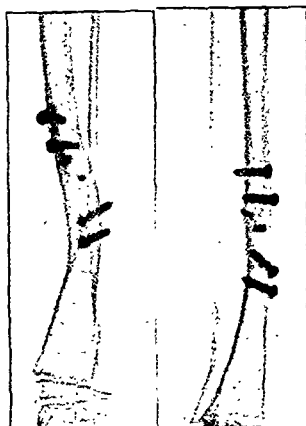


FIG. 4 (7.10.45).—Showing graft fixed by four vitallium screws.

November 1943: Admitted to Royal National Orthopædic Hospital, Stanmore, under my care.

February 1944: Bone grafting from right tibia fixed with four vitallium screws. Some sclerosed bone removed at the site of the pseudarthrosis. Lower end of fibula osteotomized.

July 1945: Caliper with moulded leather leg piece supplied. Discharged home.

October 1945: Upper two screws subcutaneous and painful.

November 1945: Upper two screws removed.

May 1946: Caliper omitted. Moulded leather below-knee splint substituted.

September 1946: Readmitted to Royal National Orthopædic Hospital, Stanmore, on

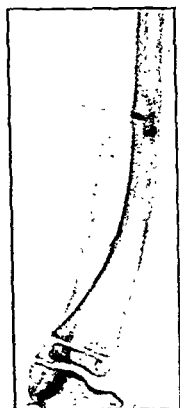


FIG. 5 (22.4.47).—Incomplete fracture without displacement.



FIG. 6 (5.8.47).—Cyst formation at site of fracture with displacement.

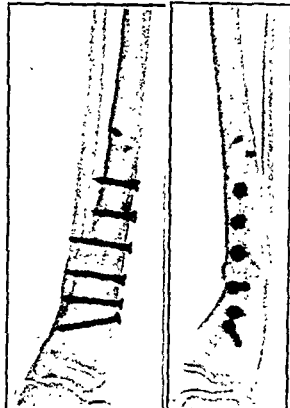


FIG. 7 (14.4.48).—Graft fixed by six vitallium screws, cyst cavity filled by bone chips.

account of pain in left leg following a fall three days previously. X-ray showed crack along the line of lowest screw.

October 1946: Lower two screws removed. Bone drilled at site of crack.

December 1946: Discharged wearing instrument.

April 1947: Fell off see-saw injuring left leg. X-ray shows small crack in left tibia below area of sclerosed bone, previous osteotomy and fracture. Below-knee walking plaster applied.

August 1947: Readmitted to Royal National Orthopædic Hospital, Stanmore. X-ray shows complete fracture of the left tibia with displacement and cyst formation (fig. 6). Clinically non-union was obvious but it was noticeable that there was singularly little pain or tenderness.

Operation.—Bone graft from tibia, fixing graft with six vitallium screws. Cyst curetted and tibial chips used to fill it. Above-knee plaster.

January 1948: Discharged home in plaster.

April 1948: Readmitted to Royal National Orthopædic Hospital, Stanmore.

Present state.—Bony union tibia and fibula with some angulation and sclerosis at fracture site. Left leg is $\frac{1}{2}$ in. short, foot is small and in some calcaneus.

May 1948: Screws removed.

Fracture of Femoral Neck Treated with a Godoy-Moreira Stud Bolt Screw.—J. D. CRONIN, F.R.C.S.

5.5.48: Mrs. L. B., aged 72. Was admitted to the Prince of Wales' Hospital with a history of having stumbled and hurt her right hip. She was unable to walk and complained of pain in the region of the hip-joint.

On examination.—External rotation deformity of right lower limb and tenderness over the neck of the femur.

X-ray: Transcervical fracture of the neck of the femur (right).

Operation (7.5.48).—Epidural anaesthesia; 4 in. longitudinal incision over the lateral aspect of the greater trochanter after reduction of fracture under X-ray control. Guide wire inserted into head and neck of femur in optimum position under X-ray control. Channel drilled through neck and head of femur with cannulated drill ($\frac{1}{4}$ in.) threaded over guide wire. Godoy-Moreira stud bolt screwed into head of femur. X-ray verified posi-



FIG. 1.

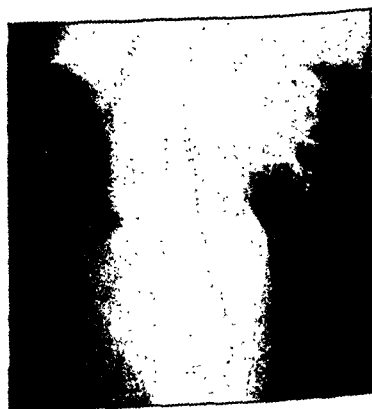


FIG. 2.

tion of screw bolt. Collar and nut applied to stud bolt and fracture powerfully impacted by tightening up. Wound closed. Uneventful recovery (figs. 1 and 2).

Two weeks after operation active movements of right hip-joint 45 degrees flexion, 35 degrees abduction, 30 degrees internal rotation, and 40 degrees external rotation.

Osteochondral Fracture of the Patella.—J. S. BATCHELOR, F.R.C.S.



FIG. 1.

On February 11, 1948, the patient, a lad aged 16 years, fell a short distance from a ladder, injuring his left knee. On examination the following day there was a large hæmarthrosis and joint movements were limited and painful. The collateral and cruciate ligaments were intact. X-ray examination (see fig. 1) revealed the presence of two loose bodies lying in the anterior compartment of the joint.

An arthrotomy was performed on March 16. A large fragment of articular cartilage with a thin layer of underlying bone was found loose in the joint cavity, with two smaller cartilaginous fragments. Examination of the patella showed that these fragments had come from the inferior part of its articular surface. There was no evidence of any damage to the femoral condyles.

The mechanism of injury was, no doubt, similar to that described by Coleman (*J. Bone Jt. Surg.*, 1948, 30B, 153). This consists essentially of a lateral subluxation of the patella, which probably occurred in this case whilst the knee was in a position of flexion and valgus. The inner border of the patella is caught by

the margin of the lateral femoral condyle and the fracture is produced by the tangential force applied by the pull of the quadriceps during the return of the patella to its normal position.

Actinomycosis Simulating Osteitis of the Pelvis.—J. S. BATCHELOR, F.R.C.S.

8.10.47: Housewife, aged 40. Admitted to hospital, 1947, with a history of pain in the region of the right iliac crest for three weeks. She looked ill and had a temperature of 101.2°, pulse 130. There was a large, fluctuating, tender swelling over the right iliac crest with marked induration of the tissues in the flank and iliac fossa. A diagnosis of osteitis of the pelvis was made.

The abscess was incised and over a pint of foul-smelling pus was evacuated. Exploration showed that the abscess cavity extended into the retroperitoneal tissues of the iliac fossa, but there was no evidence of bony disease. The cavity was packed with vaseline gauze and penicillin therapy instituted. Culture of the pus yielded a heavy growth of coliform organisms and a scanty growth of non-hæmolytic streptococci.

Following operation the induration of the tissues diminished considerably but there was a persistent discharge of pus from the abscess. Further X-ray examination did not reveal any evidence of bone infection.

On November 15 the patient's general condition had improved and she was allowed to go home. There was still a free discharge of pus from two or three sinuses in the region of the incision, and a diagnosis of actinomycosis was entertained at this time.

13.1.48: Patient readmitted. Her general condition was satisfactory but the sinuses were still discharging freely and there was a hard, tender swelling palpable in the right iliac fossa. Further X-ray examination showed no evidence of bony disease. By the end of January the mass in the right iliac fossa had increased in size and now extended into the right loin. On February 19 the sinuses were explored; a large abscess cavity extending into the true pelvis and filled with gelatinous granulation tissue and pus was found. Following this operation the pus was examined on numerous occasions for actinomycosis with negative results until, on April 15, the Department of Medical Mycology, London School of Hygiene and Tropical Medicine, confirmed the presence of *Actinomyces bovis*.

Since the operation in February, penicillin, 200,000 units eight-hourly, has been administered. There has been a slow but steady improvement in the local condition and the discharge from the sinuses is slowly diminishing.

Tomography in Surgical Tuberculosis

By VINCENT SNELL, F.R.C.S.

TOMOGRAPHY is now of established value in pulmonary tuberculosis, but its value in "surgical tuberculosis" is still undecided. A number of cases have been investigated at Harefield where patients with combined pulmonary and surgical tuberculosis are under treatment, and we have reached the following conclusions, which we feel may be of use.

Tuberculosis of the spine.—Tomography is of considerable assistance in judging the extent

account of pain in left leg following a fall three days previously. X-ray showed crack along the line of lowest screw.

October 1946: Lower two screws removed. Bone drilled at site of crack.

December 1946: Discharged wearing instrument.

April 1947: Fell off see-saw injuring left leg. X-ray shows small crack in left tibia below area of sclerosed bone, previous osteotomy and fracture. Below-knee walking plaster applied.

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FIG. 1.



FIG. 2.

tion of screw bolt. Collar and nut applied to stud bolt and fracture powerfully impacted by tightening up. Wound closed. Uneventful recovery (figs. 1 and 2).

Two weeks after operation active movements of right hip-joint 45 degrees flexion, 35 degrees abduction, 30 degrees internal rotation, and 40 degrees external rotation.

and in front of it is poorer than expected from the plain film. There is also cavitation of the lower half of D.7. and extensive disease involving the adjacent portions of D.9 and D.10 (figs. 1a and 1b).

CASE II.—S. S., female, aged 26. Bilateral pulmonary disease. Plain X-ray (fig. 2) shows involvement of D.6 with loss of joint space above. D.5 shows a number of shadows the situation of which is uncertain.

Tomogram (fig. 2a) shows involvement of D.3, 4, 5, 6 and 8.

In this case it would never have been possible to determine the situation and degree of the bone involvement without tomography.

CASE III.—J. P., male, aged 22. Plain X-ray (fig. 3)—lateral view of D.10 is obscured by the diaphragm. Tomogram (fig. 3a) shows the cavity to be considerably larger and the cartilage and disc are entirely destroyed.



FIG. 3.—Plain view.



FIG. 3A.—Tomogram, disease more extensive than expected.

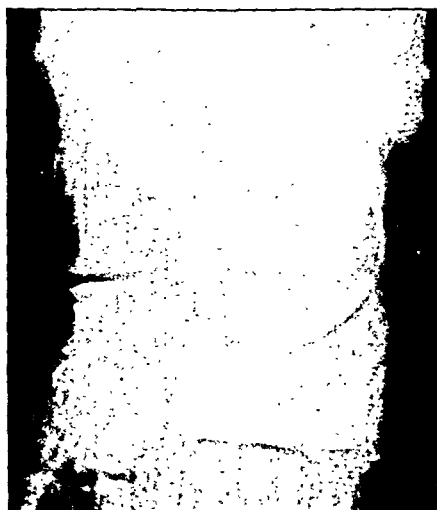


FIG. 4.—Tarsal Scaphoid. Plain view.

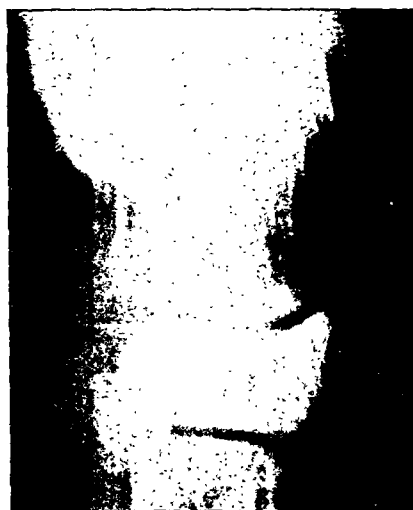


FIG. 4A. Tomogram.

of bone destruction and the number of vertebræ involved. This particularly applies to the lower cervical and upper dorsal vertebræ, and also to the lower dorsal vertebræ where the structures of the shoulder and the diaphragm respectively may make plain radiographs difficult to interpret.

It is of value throughout the dorsal spine when pulmonary disease is present. In such cases it is often uncertain whether markings on the radiographs are in the bone or the overlying lung tissue.

CASE I.—A. L., female, aged 28. Bilateral pulmonary disease. Plain lateral view shows collapse of D.8 and D.9 with cavitation of posterior two-third of both bodies (fig. 1). Tomograms confirm the collapse; they show the cavity to be larger than suspected. The bone reaction surrounding the cavity



FIG. 1.—Plain view shows disease of D.8, D.9.

FIGS. 1A and 1B.—Tomograms show disease of D.7, 8, 9 and 10. The posterior wall of the cavity is very thin.



FIG. 2.—Plain view shows two vertebræ affected.

FIG. 2A.—Tomogram (part of which is reproduced above) shows five vertebræ affected.

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FIG. 3.—Plain view.



FIG. 3A.—Tomogram, disease more extensive than expected.

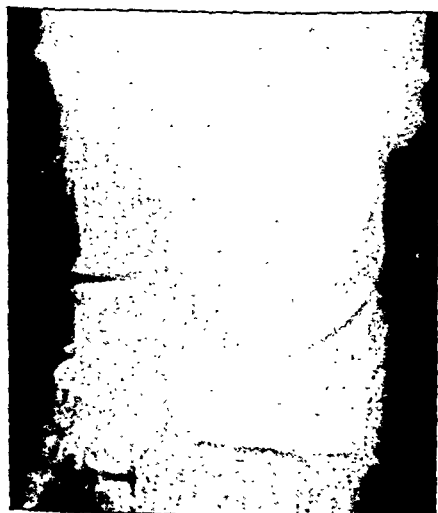


FIG. 4.—Tarsal Scaphoid. Plain view.



FIG. 4A. Tomogram.

In other regions of the spine tomography is of little value. In the cervical region and the lumbar region the additional evidence gained is not justified by the expense. In the lumbosacral region it is ineffective owing to the degree of penetration required.

Tuberculosis of other bones and joints.—There is little advantage in tomography compared with plain radiographs to compensate for the added expense.

CASE IV.—N. P., male, aged 16. Tomograms of the tarsal scaphoid show cavitation, the largest cavity extending into the joint behind. This is quite clearly shown in one plain view (fig. 4) whereas at least three tomograms must be taken to obtain a comparable result (see fig. 4a).

[July 10, 1948]

MEETING HELD AT ESSEX COUNTY COUNCIL HOSPITAL, BLACK NOTLEY

Tomography of Bones and Joints

By FRANKLIN G. WOOD, M.B., D.M.R.E.

In this paper the value of tomography in the X-ray examination of the spine, ribs, sternum and hip-joints was discussed, the skull being omitted.

Since the introduction of the modern tomography by Grossmann of Berlin in 1935, the method has been applied very generally to the lungs, especially in the demonstration of cavities, but it has not been used universally for bone conditions apart from a few workers who have become interested in the method and convinced of its value.

It is not proposed to go into the theory of tomography in any detail except in regard to



FIG. 1.

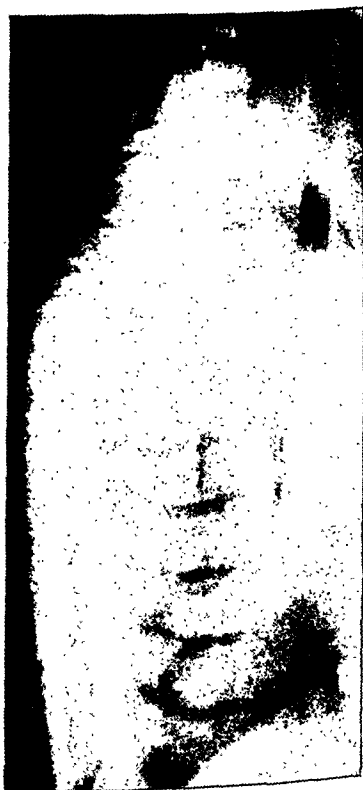


FIG. 2.

the question of the thickness of the section made; or put in another way, how far can objects be blurred out by the movement of the tube? This will depend firstly on their position relative to the line of travel, and secondly on the density of the shadow they cast in the film. The best effect is obtained in the case of a long bone when the long axis of the bone lies at

right angles to the line of travel; thus when the tube runs lengthways to the body, the ribs are fairly easily blotted out. On the other hand, when the long axis of the bone lies parallel to the line of travel, the structure tends to be drawn out into straight lines, which persist in several sections and tend to spoil the radiographic appearance. As regards the density of the shadow, soft structures, such as the lungs, are blurred very easily. Dense structures, such as calcified nodes and calcified glands, blur with difficulty, and tend to appear in more than one section.

Tomograms of the spine.—In the case of children the difficulty experienced in ordinary radiography occurs when tuberculous disease affects the lower cervical and upper dorsal vertebrae. In such a condition the child may be unable to sit up, and lies with the shoulders hunched, and the neck rigid; ordinary radiographs will fail to show the extent of the disease. By tomography this may readily be shown. Fig. 1 shows the lateral film of a child aged 2½ years, suffering from tuberculous disease of the first four dorsal vertebrae. The film was taken shortly after admission, and was the best view we were able to obtain by ordinary methods. The area of disease is very poorly defined. In the lateral tomogram, fig. 2, taken at a later date, the extent of the disease is very clearly seen. There is caries of the first four dorsal vertebrae with considerable bone destruction and an unstable spine.

As regards the upper cervical region, it can of course be shown successfully in a lateral film, but the antero-posterior view may be very difficult owing to the lower jaw, which obscures this area. A view through the mouth is difficult to obtain, especially where abscess or dislocation is present. Tomograms made in the antero-posterior position will, however, give a reasonable picture of the region.

In the adult we have used tomography more for the X-ray examination of the thoracic spine, partly as an aid in the differential diagnosis of new growth and tuberculous disease, and also to show the condition of the spinal canal in patients with actual or threatened paraplegia. In such a patient, where there is usually marked kyphosis and considerable bone changes, the spinal canal cannot be seen in the ordinary films. By tomography a much clearer picture is obtained. Also in radiographs of the spine, as indeed elsewhere in the body, there is usually more disease present than is suspected from examination of the ordinary films. Thus, if tomograms are made of the dorsal spine, areas of disease may be disclosed which were not clearly shown in the routine films.

Ribs.—Tumours of the ribs can be demonstrated in greater detail by tomography than by any other method. The patient is turned so that the affected portion of the rib lies parallel to the top of the X-ray couch, and sections are made at the appropriate level.



Sternum.—The sterno-clavicular joints may be very easily shown by the method used for routine lung tomography with the patient either prone or supine. This will show both sterno-clavicular joints and the manubrium sterni. The sternum itself is one of the most elusive bones from the radiologist's point of view. In the lateral position fairly good definition of the sternum may be obtained, unless the bone is depressed and lies in a groove, when it will be overlapped by the ribs. Other views may be taken in one of the oblique positions, with varying success as the ribs and mediastinal shadows obscure the picture. Tomography solves the problem because the rib shadows can be obliterated, and by careful positioning the sternum may be shown unobscured. The patient is placed face downwards in the left semi-oblique position and rotated so that the sternum is 5 to 7 cm. from the table. The tube is angled 10 degrees to the right, and the cassette moved 3 in. to the right in compensation. The central ray is directed just to the right of the spine. In small children the tube tilt is not recommended. By this means quite a good view of the whole of the sternum can be obtained in most cases. Fig. 3 shows a tomogram of the sternum of a boy aged 12½. It will be noticed that the first and second segments of the body are in process of uniting, whilst the second and third segments have already fused. Consideration of a short series of tomograms of the sternum in children suggests that union of these segments takes place earlier than is commonly supposed, and is complete in the case of the first and second by puberty, whilst the second and third segments unite about two years before this.

Hip-joints.—It is not claimed that tomography has any great contribution to make to the radiology of the hip-joint, but it may be used to show tuberculous foci in the acetabulum or neck of the femur in conjunction with the usual anteroposterior and lateral films.

FIG. 3.

The Late Results of Tuberculosis of the Spine in Children, with Special Reference to Spinal Grafting

By D. M. DUNN, F.R.C.S.

THE total number of cases under the age of 15, and of which a reasonably satisfactory follow-up is available is 84—not all of these had all their treatment at Black Notley. Four of these cases had demonstrable radiological lesions in two distinct areas of the spine, making the total number of lesions 88. In the tables which follow the number of lesions is considered and not the number of patients. Moreover, a case may occur in both the non-grafted series as a failure of conservative treatment and later in the grafted series.

Fifteen of these cases had spinal fusion of the Albee type but not all were operated upon in this hospital. Some had their graft at the end of the first period of conservative treatment, others only after two, or even three attempts to arrest the disease by recumbency. In some cases an attempt was made to fuse the spinous processes only of the affected vertebrae, and in others to include the spinous processes of the bodies above and below the affected area.

In dividing the cases into satisfactory and unsatisfactory results, I have been guided entirely as to whether, after an adequate period of conservative treatment, the patient, having been discharged from hospital as clinically quiescent, had or had not to be re-admitted because of further symptoms referable to the spinal lesion.

The degrees of deformity have been assessed in three grades—slight, being those with or no deformity up to 45 degrees; moderate, being those with from 45 to 90 degrees deformity; and gross, being those with deformity of more than 90 degrees.

TABLE I.

Level of lesion			Average duration of primary treatment in years	Length of follow-up in years		
				Max.	Min.	Average
Cervical and upper dorsal						
Total 10	Satisfactory	9	2 2/12 Died	11	1 4/12	5 4/12
	Unsatisfactory	1				
Dorsal and dorso-lumbar						
Total 45	Satisfactory	13	2 4/12	9	1 2/12	4 3/12
	Unsatisfactory	32	2 3/12	15	1	7 3/12
Lumbar						
Total 24	Satisfactory	18	2 2/12	9	1 2/12	4 3/12
	Unsatisfactory	6	2	15	1	7 3/12

It will be noticed that the average follow-up period of unsatisfactory results is appreciably longer than the satisfactory results, indicating the late incidence of further activation.

TABLE II.—MORTALITY

	Total No. cases	Died	%
Non-graft	79	9	11.4
Graft	15	3	20

Of the cases not grafted, except for one boy who died at the age of about 25 with Parkinson's disease, not one survived beyond the age of 7 and five had died at the age of 4 or sooner. Seven of these cases died of tuberculous meningitis and one of military tuberculosis. Two developed the meningitis within three months of operation on a tuberculous focus. Two others died following a mis-diagnosis and failed initial treatment. It seems, therefore, that if the child survives the bacillæmic stage of the illness till he is 7 or 8 years old he is unlikely to die as a result of his tuberculosis. Of the three cases which were grafted and later died, one was grafted at the age of 9 and died of pulmonary tuberculosis at the age of 17. Another was grafted at the age of 7, but at about the age of 11 developed a partial paraplegia. This fluctuated considerably in degree, and when he was 14 a costotransversectomy was performed and the vertebral bodies curetted, bone chips from the adjacent rib being packed into the affected region. This child died of tuberculous meningitis about three months later. The third case died at home, aged 19; the cause of

death is unrecorded, but she had been discharged three years earlier with an unrelieved paraplegia.

Of the ungrafted cases 29, i.e. 36%, were readmitted, with the following leading symptoms—8 had local reactivation, 8 had increasing deformity, 7 had paraplegia, 3 had sinuses, 2 had abscesses and 1 had urinary tuberculosis. Of the 15 grafted cases 6, or 40% were readmitted—4 had paraplegia, 3 had increasing deformity, 1 had sinuses and 1 had pulmonary tuberculosis. The rate for readmission and the reason for readmission are similar in the grafted and the ungrafted cases. Moreover, it seems to make little difference whether the graft had been done at the end of the initial treatment or later. Of the 7 cases on which bone grafting was performed at the end of the first period of conservative treatment, 3 were readmitted, of which one later died. Furthermore, it can be shown that of the grafted cases which had a satisfactory result, in several the graft was unsatisfactory from a mechanical point of view; in fact the main function of a posterior bone graft seems to be to ensure that anterior bony fusion does not occur between the bodies, which is the patient's main insurance against reactivation.

Of the 9 cases grafted and appearing in the table as a satisfactory result, in one case the graft was too low and the degree of deformity increased from 50 to about 85 degrees. In another case the graft failed to unite at the upper part of the diseased area and there was some increase of deformity. In a third there was complete failure of the fusion and in a fourth the graft fractured near its upper end. Of the unsatisfactory results following grafts, two had increasing deformity associated with paraplegia since the graft, and a third had increasing deformity and abscess formation.

TABLE III.—DEGREE OF DEFORMITY. UNGRAFTED

			0-45 degrees	45-90 degrees	90+ degrees	Unknown
Cervical and upper dorsal	} Total 10	Satisfactory ..	7	1	1	1 (died)
		Unsatisfactory	—	—	—	
Dorsal and lumbo-dorsal	} Total 45	Satisfactory ..	5	5	3	0
		Unsatisfactory	—	5	19	8
Lumbar	} Total 24	Satisfactory ..	12	3	0	3
		Unsatisfactory	2	2	1	1

TABLE IV.—DEGREE OF DEFORMITY. GRAFTED*

			0-45 degrees	45-90 degrees	90+ degrees
Dorsal and upper lumbar	(a) 1st admission	Satisfactory ..	—	2	0
		Unsatisfactory	—	1	1
	(b) Later	Satisfactory ..	—	1	2
		Unsatisfactory	—	—	2
Lumbar	(a) 1st admission	Satisfactory ..	2	—	—
		Unsatisfactory	1	—	—
	(b) Later	Satisfactory ..	1	—	1
		Unsatisfactory	—	—	—

*In one unsatisfactory case the degree of deformity is not recorded.

TABLE V.—TYPE OF ANTERIOR FUSION

			Bone	Fibrous	Unknown
Cervical and upper dorsal	Satisfactory		2	3	4
	Unsatisfactory		—	—	—
Dorsal and lumbo-dorsal	Satisfactory	No graft	4	5	4
		Graft ..	0	5	0
	Unsatisfactory	No graft	0	12	20
		Graft ..	0	2	2
Lumbar	Satisfactory	No graft	7	5	6
		Graft ..	1	3	1
	Unsatisfactory	No graft	0	6	1
		Graft ..	0	1	1

In only one case that was grafted did anterior bony fusion occur. None of the cases with bony fusion gave an unsatisfactory result.

TABLE VI.—AVERAGE NUMBER OF BODIES INVOLVED

				C. and Upper D.	D. and D. L.	L.
Grafts	{ Satisfactory	—	4.8	2.5
	{ Unsatisfactory	—	4.3	2.5
Non-grafts	{ Satisfactory	3.6	3.3	2.3
	{ Unsatisfactory	4.0	4.6	2.5

It will be seen that the average number of bodies affected is very little greater in the grafted than in the ungrafted series. In other words, the poor results of grafting cannot be explained adequately by saying that the worst cases only were grafted.

SUMMARY

There is no evidence here that spine grafting in children reduces the mortality or the incidence of readmission because of complications or later reactivation, nor does it control the development of a kyphosis. Though the number of cases is few, it does suggest that grafting prevents the formation of anterior bony fusion between the vertebral bodies. What then is needed—bigger and better grafts? It seems that this would be more likely to keep the disease in the bodies active rather than preserve its quiescence. Or should the operation be directed against the disease focus in the bodies in an attempt to eradicate the caseous material and sequestered bone and replace it with cancellous bone chips? Obviously there is a greater operative risk with this type of operation than with the Albee grafts, though this could be lessened by making use of bone from a bone bank. Moreover there seems to be a very definite risk of tuberculous meningitis following a direct approach to the bodies, which must necessarily cut across the perivertebral plexus of veins; there is also some risk of tuberculous pleurisy. Can we yet say that the streptomycin treatment of meningitis is sufficiently satisfactory to justify the risk? Until this is so, the indication is for earlier diagnosis and immobilization until the bacillæmic stage of the disease is over and the refraining from a posterior graft which is all too likely to prevent anterior consolidation of the bodies.

Section of Pædiatrics

President—W. G. WYLLIE, M.D., F.R.C.P.

[May 22, 1948]

MEETING HELD AT THE ROYAL INFIRMARY, CARDIFF

Periodic Familial Paralysis.—W. G. WYLLIE, M.D., F.R.C.P., and A. G. WATKINS, F.R.C.P.

Mrs. M. has had attacks of paralysis since 3 years old, but of late the attacks have been lasting more or less continuously for three to four days or even up to a week. She complains of aching and weakness of the muscles of the legs; the arms are unaffected.

April 1946: Blood potassium 18.9 mg. %.

Mrs. M. says she is worse after taking potassium.

D. M., male, aged 5½ years. Mrs. M.'s son. Becomes "completely helpless" at times. Attacks last ten to fifteen minutes and may be brought on by sudden cooling after exercise or after prolonged rest. Onset at 8 months old.

J. M., female, aged 2½ years. Mrs. M.'s daughter. Free from attacks. (see fig. 1).

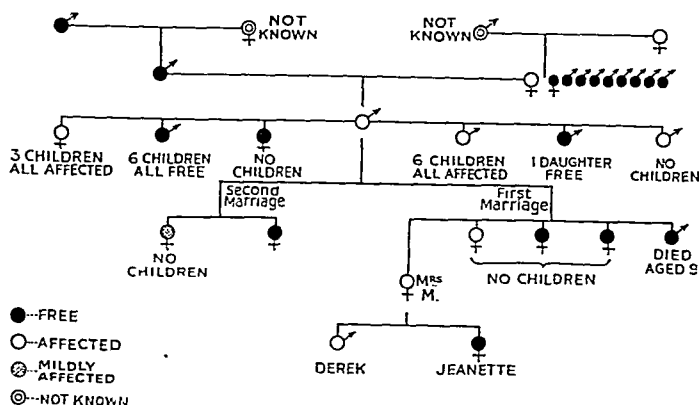


FIG. 1.—Periodic familial paralysis.

Cerebellar Atrophy.—J. D. SPILLANE, M.D.

Miss I. R., aged 16 years. Admitted to this hospital in March 1948. Symptoms began in April 1946 with shakiness of the left hand followed shortly afterwards by changes in speech. An ataxia of all voluntary movement gradually spread and increased in intensity producing her present state of marked asynergia.

Family history.—The maternal grandfather committed suicide and his brother was psychotic. There was no other family neuropathy.

On examination the general state of nutrition was good. There was a gross speech defect making her almost unintelligible. She showed a spontaneous rotatory coarse nystagmus, and a gross cerebellar ataxia of gait and all voluntary movement. She had all the other signs of a pure cerebellar lesion. There was no evidence of involvement of the pyramidal or posterior column tracts. Lumbar puncture showed no abnormality of itself or in the fluid. W.R. was negative in blood and cerebrospinal fluid. Air encephalography showed a little excess air over the cerebral cortex with cerebellar atrophy as judged by increased size of the fourth ventricle, the excess of inter-folial air and a general increase of air in the posterior cranial fossa.

Female Epispadias.—R. A. MOGG, F.R.C.S.

S. H., aged 6 years. Incontinence of urine since birth. No relevant past history.

8.9.47: General condition good. Excoriation of vulva and vagina. Abdomen normal. Clitoris split along the dorsum; the urethra shows the female type of epispadias. Palpable depression in the region of the mons pubis due to separation of the symphysis pubis.

Cystoscopy.—No resistance to passage of cystoscope. Bladder sphincter appeared to be deficient. Bladder normal apart from gross congestion of trigone.

Treatment.—Bilateral transplantation of ureters performed in two stages using the extra-peritoneal technique. Convalescence uneventful. Rectal control good.

DEC.—PÆDIAT. 1

Complete Double Right Ureter with Ectopic Insertion of the Upper Ureter. Ureterocele of the Ectopic Ureter causing Left Hydro-ureter and Hydronephrosis.—R. A. MOGG, F.R.C.S.

J. C., male, aged 9 years.

First seen at the age of 5 years suffering from pyuria, hæmaturia and albuminuria following measles. Improved but relapsed. I.V.P. showed dilatation of left ureter and renal pelvis and no secretion from the right side after one and a half hours.

Cystoscopy 23.10.46 showed an unexplained elevation of the trigone; the ureteric orifices were normal in position but patulous and could not be catheterized.

Exploration of bladder 30.10.46 showed a greatly hypertrophied wall and a complete double ureter on the right side, the upper ureter opening ectopically at the bladder neck with an associated ureterocele. The whole of the trigonal mucosa was elevated by this dilated ectopic ureter to such a degree that it obstructed the left ureteric orifice causing hydro-ureter. The ureterocele and the lower part of the right ectopic ureter were resected, indwelling ureteric catheters were passed up the right ureters, pyelography was performed and the bladder closed round a suprapubic tube.

Convalescence was uneventful and he was discharged symptom free. There is an occasional *B. coli* infection of the urine; there was a mild hæmaturia on 25.3.47, but the child remains fit and well and attends school regularly.

Subdural Hæmatoma—Two Cases.—H. R. I. WOLFE, F.R.C.S. (Surgical Unit).

CASE I.—M. E., male, aged 13 months, was referred as a case of hydrocephalus.

History.—Fourth child of rhesus positive parents. Both brothers alive and well. Sister alive but thought to be a mongol. Full-term pregnancy, normal delivery. Slightly jaundiced at birth but this rapidly cleared. At age of 6 months it was noticed the head was abnormally large. Progress had been otherwise normal and there was no history of injury to the head.

Clinically.—Pale, anæmic and fretful child who could not sit up without support (*see fig.*). The head was abnormally large—maximum circumference 23 in.—and the anterior fontanelle was enlarged and tense. Intelligence did not appear to be impaired. No other abnormal physical signs.

Special investigations.—R.B.C. 2,620,000. Hb 28%. C.I. 0.53. W.B.C. 8,000. Platelets 80,000. Clotting time 6 minutes.

Slightly raised resistance of red cells to hypotonic saline. W.R. negative. C.S.F.—Clear fluid, pressure 300 mm. 2 lymphocytes per c.mm. Protein 40 mg.%. R.B.C. 146 per c.mm.

Encephalography: Symmetrical slight dilatation of ventricular system which appears to be displaced downwards.

Bilateral subdural tap through anterior fontanelle.—Subdural collection of orange fluid on right side: protein content 4,400 mg.%. Subdural collection of brown fluid on left side: protein content 5,600 mg.%.

Treatment.—By transfusion, fersolate, vitamin C and further subdural taps.

Operation (Professor Lambert Rogers, 31.1.48).—A 1½ in. trephine disc was removed just anterior to the parietal eminence on the right side and the dura opened. A thick green membrane lightly adherent to the dura was incised and removed. Dark blood-stained fluid was evacuated from the subdural space. A thin smooth green membrane over the cerebral cortex was incised and removed. The underlying cortex appeared normal. A small rubber tube was placed through the centre of the trephine disc which was then replaced and the wound closed.

Convalescence was uneventful and the patient discharged on 10.3.48. Readmitted 8.5.48. Circumference of skull 22 in. General condition excellent. Bright, intelligent child. Able to walk.

ADDENDUM

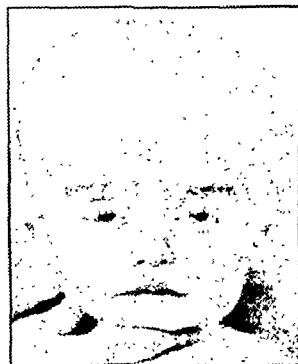
Operation (Professor Lambert Rogers, 30.6.48).—Operation carried out on the left side similar to that on the right. Subdural collection of brown fluid and blood clot removed. Membranes removed. Cavity filled with Ringer's solution. Bone disc replaced and wound closed without drainage.

Convalescence uneventful and patient discharged 12.7.48.

Follow-up, 18.12.48: Very satisfactory progress. The child is of normal intelligence.

CASE II.—T.S., male, aged 8 months.

History.—Father, mother, brother and sister alive and well. Full term pregnancy, normal delivery, birth-weight 7½ lb. "Operation for gland of neck" when 3 months old.



M. E., aged 13 months.

Admitted to City Hospital, Plymouth, when 7 months old in status epilepticus. Prior to admission feeds had been taken reluctantly and there had been copious vomiting. No history of injury to head.

Examination.—Bilateral retinal hæmorrhages. Minor degree of spinal rigidity and hydrocephalus (circumference of head 18½ in.).

Investigations.—Lumbar puncture: Xanthochromic fluid not under pressure. Protein 45 mg. %. Globulin—faint trace. R.B.C. 50. Lymphocytes 12.

Blood W.B.C. 29,600. Platelet count and bleeding and clotting time normal.

Wassermann reaction of blood and C.S.F. negative.

Progress.—Epileptic fits ceased three hours after admission. Occasional generalized twitching during next two weeks, when right-sided hemiplegia noted. Signs of increased intracranial pressure—papillædema and bulging of anterior fontanelle—present on admission. These subsided and child regained consciousness five days after admission, but was apparently blind.

Admitted to Royal Infirmary, Cardiff, when 8 months old.

Examination.—Healthy, good-tempered, rosy-cheeked child (see fig.). Slight eczema of scalp. Head large. Anterior fontanelle open, tense and bulging slightly. Right-sided hemiparesis. Pupils equal and react to light. No ophthalmoplegia. Child apparently blind, for gaze does not fix on bright light or feeding bottle and no reaction to brisk movement in line of vision. Optic discs flat and of fairly normal colour. Extensive central area of retinal hæmorrhage in right eye.

Investigations.—Bilateral subdural tap through anterior fontanelle. Right side—dark blood-stained fluid, protein 1,600 mg. %. Left side—orange fluid, protein 1,500 mg. %. Blood-count: R.B.C. 2,690,000. Ascorbic acid 0.6 mg. %.

Treatment.—Transfusion, fersolate and vitamin C, and repeated bilateral subdural tapping.



T. S., aged 8 months.

ADDENDUM

Operation (Mr. Wolfe, 3.7.48).—Removal of trephine disc in left parietal region. Dura incised and blue-grey external membrane stripped and removed from dura. Cyst emptied, and thin smooth greenish inner membrane removed from cortex. The inner membrane stripped with ease except at one point where an oozing vascular adhesion was found to traverse the subdural space from the inner to the outer membrane 1½ in. lateral to the superior longitudinal sinus. Portion of inner membrane the size of a postage stamp was left adherent to the cortex at the base of this adhesion, which was then severed and removed with a portion of the outer membrane for histology. The cerebral cortex, initially pale and rather flattened, within a minute following the removal of the inner membrane became vascular and of normal appearance. The cavity was filled with Ringer's solution, the dural defect closed, the bone disc replaced and the wound sutured without drainage.

Convalescence uneventful.

Pathological report on portion of outer wall of subdural cyst with vascular pedicle: The tissue is composed of proliferating blood-vessels with a stroma of collagen. Around some of the vessels is a concentric proliferation of cells giving the appearance similar to that seen in a meningioma. The cyst has a dense fibrous wall in which there are deposits of hæmosiderin. The condition is possibly a hæmangioma of the meninges, but it probably represents organization in the wall of a subdural hæmatoma.

14.8.48: *Operation* carried out on right side similar to that on left. A thick gelatinous green outer membrane was stripped without difficulty from the dura. A subdural collection of dark reddish brown fluid was removed. The pearly white semi-translucent inner membrane was then removed from the cortex. Convalescence was uneventful and the patient discharged from hospital on 3.9.48.

Follow-up, 18.12.48: Satisfactory progress. There would appear to be some degree of recovery of vision for the child will now respond to the stimulus of a bright light.

Comment.—In both these cases the inner membrane of the subdural cyst was found to be semi-permeable when the cyst fluid was placed within the membrane and tested against the patient's blood. It is noteworthy that in Case I, which was referred as a case of hydrocephalus (a diagnosis which might have been accepted but for ventriculography), there were no abnormal neurological signs, and that in Case II, where the head was only slightly enlarged, neurological symptoms were pronounced.

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First seen at the age of 5 years suffering from pyuria, hæmaturia and albuminuria following measles. Improved but relapsed. I.V.P. showed dilatation of left ureter and renal pelvis and no secretion from the right side after one and a half hours.

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Convalescence was uneventful and the patient discharged on 10.3.48. Readmitted 8.5.48. Circumference of skull 22 in. General condition excellent. Bright, intelligent child. Able to walk.

ADDENDUM

Operation (Professor Lambert Rogers, 30.6.48).—Operation carried out on the left side similar to that on the right. Subdural collection of brown fluid and blood clot removed. Membranes removed. Cavity filled with Ringer's solution. Bone disc replaced and wound closed without drainage.

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History.—Father, mother, brother and sister alive and well. Full term pregnancy, normal delivery, birth-weight 7½ lb. "Operation for gland of neck" when 3 months old.

demonstrates the typical appearance of Ehlers-Danlos syndrome differing only in that there does not appear to be any crackling of the skin or a tendency to undue hæmorrhage.

The child's mother would appear to suffer in a mild degree from the same condition.

The following seven cases were shown by Dr. A. G. WATKINS and the Staff of the Pædiatric Department, Cardiff Royal Infirmary.

Cases I to III. Chondrodysplasia in a Family of Three Children.

M. A., male, aged 8 years. Height 3 ft. 2 in. Weight 38½ lb.

J. A., female, aged 7 years. Height 2 ft. 6½ in. Weight 24 lb.

J. A., male, aged 5½ years. Height 2 ft. 8 in. Weight 26 lb.

No other children. Parents healthy; no consanguinity. Family history nil. All three children normal mentally and of good general health.

X-ray films demonstrated typical bony changes.

Case IV. Calcinosis Universalis.

R. G., male, aged 6½ years.

Lumps in lower end of right upper arm first noted at 2 years of age. They later developed on left arm and behind knees. The lumps vary in size and almost disappear at times; there is no discharge.

A small patch of dermatitis is present on outer side of right arm. General health good. Family history: nothing relevant.

Blood-count normal. Serum calcium 11.2 mg.%; serum phosphate 5 mg.%; alkaline phosphatase 24 units.

X-ray films demonstrated calcified subcutaneous areas opposite lower end of both humeri, also large calcified area over left psoas muscle.

Case V. Hypertrophy of Left leg.

F. B., male, aged 6½ years. Left leg first noticed to be bigger than right at 1 year. Increasing disability and unable to walk far.

	Left	Right
Circumference of leg 3 in. above patella ..	12 in.	12 in.
Circumference of leg 5 in. below patella ..	10½ in.	8½ in.
Circumference of leg at ankle ..	8½ in.	7 in.
Anterior iliac spine to patella ..	11½ in.	10½ in.
Tibial spine to lateral malleolus ..	13 in.	11 in.

No alteration in limb temperature. No alteration in cardiac rate on occluding left femoral. Blood-pressure equal in both legs. Femoral vein puncture shows equal oxygenation in both legs. X-ray films demonstrated simple enlargement of femur and tibia.

Case VI. ? Bilateral Arteriovenous Anastomosis.

E. D., female, aged 15 years.

Surface nævi on both legs extending to buttocks. Varicose veins of both legs. Intermittent swelling of feet. On two occasions discharge from pin-point openings behind right knee, ? chyle. Blood-pressure equal in both limbs. No cardiac lesion. No investigations done.

Case VII. Arteriovenous Anastomosis.

D. P., female, aged 14½ years.

First seen in May 1941 because of a "milky discharge" from the inner side of right thigh of two days' duration. The discharge was chylous fluid from a pin-point opening approximately at the apex of Scarpa's triangle. There has been no recurrence from that site but two years later she had a similar discharge *per vaginam* and this has occurred intermittently since. It is always better when she is at rest. Right leg was noted to be longer, fatter and hotter than left. Occlusion of right femoral slowed pulse after an interval of six beats.

April 1943: Subarachnoid hæmorrhage—attack while in hospital.

October 1945: Considerable lengthening of right limb with gross compensatory scoliosis. Spasticity of both limbs, more marked on right side; double Babinski. Groin temperature half a degree higher on right side.

November 1947: Blood-pressure normal and equal on both sides in arm and leg. Right leg 3 in. longer than left. Right leg 1½ in. greater in circumference than left. Right leg 5½ in. cephalic in Nélaton's line.

no abno;—PÆDIAT. 2

larged, neu.

Congenital Webbing of the Lower Limbs.—EMLYN LEWIS, F.R.C.S.

E. N., girl, aged 7 years. Referred because of inability to walk without crutches and suffering from congenital contractures of the lower limbs. The child is one of a family of four, the father has a harelip and cleft palate, and a brother a cleft palate and similar congenital web formation of the lower limbs. Patient has a bilateral incomplete harelip and a posterior two-thirds cleft palate.

The webs extend from the region of the tuber ischii down to the heels. They limit extension of the knee-joint by 40 degrees and the ankle-joints very considerably. The webs had been previously explored elsewhere and a neurovascular bundle was encountered in the free margin of the web. At operation the above findings were corroborated but in addition it was found that there were large muscle sheets extending from the tuber ischii to the heel region which were responsible for the web formation. Presumably these muscle sheets had failed to gain their intermediate attachments either below to the upper end of the tibia or above to the lower end of the femur. The muscle sheets were divided and secondarily attached to the tibia and femur in order to reproduce something like normal anatomical distribution. Z-plastics were performed on the skin folds and in this way considerable elongation obtained. After operation gradual extension of the knee-joint was obtained by means of a spring extension apparatus in order slowly to elongate the neurovascular bundle.

The patient is now able to walk unaided. The left lower limb now functions correctly and the right limb is being restored to normal position.

Following these procedures the development of the heel portion of the os calcis has been very considerable.

Leontiasis Ossea.—EMLYN LEWIS, F.R.C.S.

M. T., a boy, aged 11 years. Referred as a case of sarcoma of the right maxilla with right nasal obstruction. It was noted at this time that in addition to the swelling of the right maxilla there was also expansion of the frontal and temporo-parietal regions. Nasal obstruction was corroborated and the right eye was elevated.

X-ray examination: Bony expansion of the superior maxilla, right frontal bone and right temporal region. No other bony abnormalities were found in the long bones.

Blood: Hb and cells normal. Blood calcium 8 mg. %, phosphorus 5.5 mg. %, phosphatase 25 units.

At examination it was decided that the symptoms did not warrant operative interference, but it is proposed that when the symptoms, due to mechanical factors, warrant it, bony reduction should be carried out and specimens of the bone examined histologically.

Osteopetrosis (Marble Bones).—EMLYN LEWIS, F.R.C.S., and Pædiatric Dept.

A. W., boy, aged 9 years. Referred because of osteomyelitis of the lower jaw, which started in February 1947. Three years previously he had fractured his femur and examination showed that he had a large spleen but the blood picture was normal at that time. Routine X-ray examination revealed condition of marble bones.

X-ray examination for osteomyelitis of the jaw showed typical marble bone appearance together with extensive osteomyelitis of the right side of the mandible. Intra-oral examination showed presence of dead bone. Spleen considerably enlarged. Some ascites.

Blood examination.—R.B.C. 3,250,000; Hb 50%; C.I. 0.8; W.B.C. 12,800 (polys. 43%, lymphos. 30%, myelos. 13%, monos. 9%, eosinos. 5%). Nucleated reds 8 per 100 W.B.C. Polychromasia with stippling. Film was said to show a leuco-erythroblastic anæmia. W.R. and Kahn negative.

When operation was performed on the lower jaw it was found that the greater part of the horizontal ramus was necrotic and surrounded by a large mass of vascular fibrous bone, which when drilled produced a cloud of dust. The new bone was very brittle and fractured in removing the dead bone. The fragments were wired and the wound closed with drainage. It is interesting to note that osteomyelitis of the jaw appears to be a frequent terminal condition in these children. Presumably it arises via carious milk teeth and when combined with the relative avascular condition of the bone assumes severe proportions.

Repeated transfusions were given and his Hb is now 75% with R.B.C. 4,250,000.

Cutis Laxa.—EMLYN LEWIS, F.R.C.S.

P. T., aged 7, girl. Referred because of appearance. The girl presented a facial and neck appearance of an elderly person and it was found that she was referred to by her classmates as "Granny." A bilateral face-lifting operation was performed, which considerably improved her appearance. Since performing the operation it is apparent that she has ^{sy.} notably aged and it may be worth while repeating the surgical procedure. The skin of her ^{abdomen} ^{retched} ^{ed.}

demonstrates the typical appearance of Ehlers-Danlos syndrome differing only in that there does not appear to be any crackling of the skin or a tendency to undue hæmorrhage.

The child's mother would appear to suffer in a mild degree from the same condition.

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J. A., female, aged 7 years. Height 2 ft. 6½ in. Weight 24 lb.

J. A., male, aged 5½ years. Height 2 ft. 8 in. Weight 26 lb.

No other children. Parents healthy; no consanguinity. Family history nil. All three children normal mentally and of good general health.

X-ray films demonstrated typical bony changes.

Case IV. Calcinosis Universalis.

R. G., male, aged 6½ years.

Lumps in lower end of right upper arm first noted at 2 years of age. They later developed on left arm and behind knees. The lumps vary in size and almost disappear at times; there is no discharge.

A small patch of dermatitis is present on outer side of right arm. General health good. Family history: nothing relevant.

Blood-count normal. Serum calcium 11.2 mg.%; serum phosphate 5 mg.%; alkaline phosphatase 24 units.

X-ray films demonstrated calcified subcutaneous areas opposite lower end of both humeri, also large calcified area over left psoas muscle.

Case V. Hypertrophy of Left leg.

F. B., male, aged 6½ years. Left leg first noticed to be bigger than right at 1 year. Increasing disability and unable to walk far.

	Left	Right
Circumference of leg 3 in. above patella ..	12 in.	12 in.
Circumference of leg 5 in. below patella ..	10½ in.	8½ in.
Circumference of leg at ankle ..	8½ in.	7 in.
Anterior iliac spine to patella ..	11½ in.	10½ in.
Tibial spine to lateral malleolus ..	13 in.	11 in.

No alteration in limb temperature. No alteration in cardiac rate on occluding left femoral. Blood-pressure equal in both legs. Femoral vein puncture shows equal oxygenation in both legs. X-ray films demonstrated simple enlargement of femur and tibia.

Case VI. ? Bilateral Arteriovenous Anastomosis.

E. D., female, aged 15 years.

Surface nævi on both legs extending to buttocks. Varicose veins of both legs. Intermittent swelling of feet. On two occasions discharge from pin-point openings behind right knee, ? chyle. Blood-pressure equal in both limbs. No cardiac lesion. No investigations done.

Case VII. Arteriovenous Anastomosis.

D. P., female, aged 14½ years.

First seen in May 1941 because of a "milky discharge" from the inner side of right thigh of two days' duration. The discharge was chylous fluid from a pin-point opening approximately at the apex of Scarpa's triangle. There has been no recurrence from that site but two years later she had a similar discharge *per vaginam* and this has occurred intermittently since. It is always better when she is at rest. Right leg was noted to be longer, fatter and hotter than left. Occlusion of right femoral slowed pulse after an interval of six beats.

April 1943: Subarachnoid hæmorrhage—attack while in hospital.

October 1945: Considerable lengthening of right limb with gross compensatory scoliosis. Spasticity of both limbs, more marked on right side; double Babinski. Groin temperature half a degree higher on right side.

November 1947: Blood-pressure normal and equal on both sides in arm and leg. Right leg 3 in. longer than left. Right leg 1½ in. greater in circumference than left. Right leg 5½ in. difference in Nélaton's line.

Congenital Webbing of the Lower Limbs.—EMLYN LEWIS, F.R.C.S.

E. N., girl, aged 7 years. Referred because of inability to walk without crutches and suffering from congenital contractures of the lower limbs. The child is one of a family of four, the father has a harelip and cleft palate, and a brother a cleft palate and similar congenital web formation of the lower limbs. Patient has a bilateral incomplete harelip and a posterior two-thirds cleft palate.

The webs extend from the region of the tuber ischii down to the heels. They limit extension of the knee-joint by 40 degrees and the ankle-joints very considerably. The webs had been previously explored elsewhere and a neurovascular bundle was encountered in the free margin of the web. At operation the above findings were corroborated but in addition it was found that there were large muscle sheets extending from the tuber ischii to the heel region which were responsible for the web formation. Presumably these muscle sheets had failed to gain their intermediate attachments either below to the upper end of the tibia or above to the lower end of the femur. The muscle sheets were divided and secondarily attached to the tibia and femur in order to reproduce something like normal anatomical distribution. Z-plastics were performed on the skin folds and in this way considerable elongation obtained. After operation gradual extension of the knee-joint was obtained by means of a spring extension apparatus in order slowly to elongate the neurovascular bundle.

The patient is now able to walk unaided. The left lower limb now functions correctly and the right limb is being restored to normal position.

Following these procedures the development of the heel portion of the os calcis has been very considerable.

Leontiasis Ossea.—EMLYN LEWIS, F.R.C.S.

M. T., a boy, aged 11 years. Referred as a case of sarcoma of the right maxilla with right nasal obstruction. It was noted at this time that in addition to the swelling of the right maxilla there was also expansion of the frontal and temporo-parietal regions. Nasal obstruction was corroborated and the right eye was elevated.

X-ray examination: Bony expansion of the superior maxilla, right frontal bone and right temporal region. No other bony abnormalities were found in the long bones.

Blood: Hb and cells normal. Blood calcium 8 mg. %, phosphorus 5.5 mg. %, phosphatase 25 units.

At examination it was decided that the symptoms did not warrant operative interference, but it is proposed that when the symptoms, due to mechanical factors, warrant it, bony reduction should be carried out and specimens of the bone examined histologically.

Osteopetrosis (Marble Bones).—EMLYN LEWIS, F.R.C.S., and Pædiatric Dept.

A. W., boy, aged 9 years. Referred because of osteomyelitis of the lower jaw, which started in February 1947. Three years previously he had fractured his femur and examination showed that he had a large spleen but the blood picture was normal at that time. Routine X-ray examination revealed condition of marble bones.

X-ray examination for osteomyelitis of the jaw showed typical marble bone appearance together with extensive osteomyelitis of the right side of the mandible. Intra-oral examination showed presence of dead bone. Spleen considerably enlarged. Some ascites.

Blood examination.—R.B.C. 3,250,000; Hb 50%; C.I. 0.8; W.B.C. 12,800 (polys. 43%, lymphos. 30%, myelos. 13%, monos. 9%, eosinos. 5%). Nucleated reds 8 per 100 W.B.C. Polychromasia with stippling. Film was said to show a leuco-erythroblastic anaemia. W.R. and Kahn negative.

When operation was performed on the lower jaw it was found that the greater part of the horizontal ramus was necrotic and surrounded by a large mass of vascular fibrous bone, which when drilled produced a cloud of dust. The new bone was very brittle and fractured in removing the dead bone. The fragments were wired and the wound closed with drainage. It is interesting to note that osteomyelitis of the jaw appears to be a frequent terminal condition in these children. Presumably it arises via carious milk teeth and when combined with the relative avascular condition of the bone assumes severe proportions.

Repeated transfusions were given and his Hb is now 75% with R.B.C. 4,250,000.

Cutis Laxa.—EMLYN LEWIS, F.R.C.S.

P. T., aged 7, girl. Referred because of appearance. The girl presented a facial and neck appearance of an elderly person and it was found that she was referred to by her classmates as "Granny." A bilateral face-lifting operation was performed, which considerably improved her appearance. Since performing the operation it is apparent that she has not aged again and it may be worth while repeating the surgical procedure. The skin of her face

(1) *Death due to a "congenital defect".*—12 cases. In one case a previously symptomless infundibular cyst produced an acute fatal hydrocephalus. In another a large intrathoracic cyst was present, considered on histological grounds to be derived from enteric epithelium. The remainder of the group comprised gross cardiac defects (5), pulmonary atelectasis (3), neonatal hæmorrhagic disease (1) and an instance of asphyxiation produced by a grossly mobile tongue.

The cases thus grouped died almost exclusively in the first month of life (fig. 2) and indeed 9 of them were aged 1 week or under. Thus concentrated they represent an important proportion of the total deaths encountered in the neonatal period.

(2) *Death due to an infectious process.*—Infection was the major cause of death, accounting for about a third of all cases (fig. 3). In two-thirds of these (21 out of 30) the site of infection was respiratory (viz. upper respiratory infection (7), suppurative bronchopneumonia¹ (9) and acute interstitial pneumonia (5)).

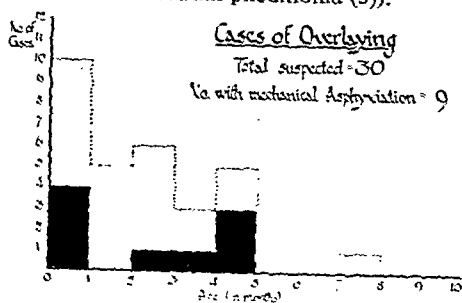


FIG. 4.

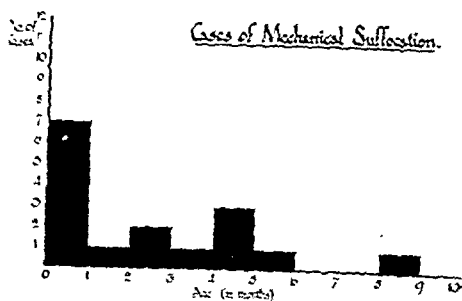


FIG. 5.

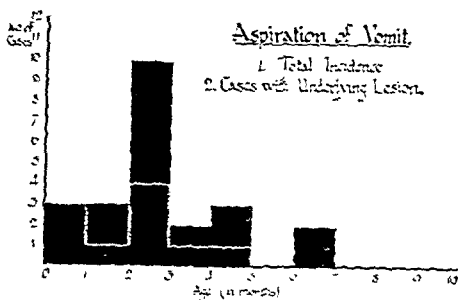


FIG. 6.

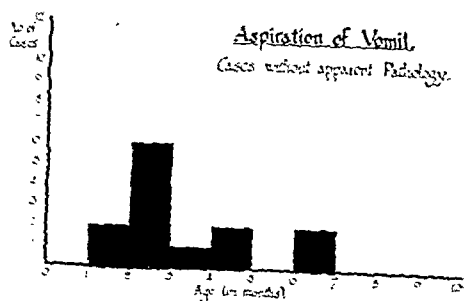


FIG. 7.

Other conditions responsible for death in this group included single cases of encephalitis, meningitis and acute hepatitis.

(3) *Death due to mechanical suffocation.*—In 30 of the cases studied, death had occurred while the infant was in a bed with one or more other occupants. At autopsy, however, only 9 of these infants presented signs of asphyxiation which could have been ascribed to overlaying—the remainder showed another adequate cause for death. The striking difference between the incidence of suspected overlaying and substantiated mechanical asphyxiation is shown in fig. 4.

The remaining 51 cases died when alone in bed, and of these 7 were considered to have died from asphyxiation as the result of pressure from bedclothes. Thus of the 81 cases investigated in this paper a total of 16 only appeared to have suffered mechanical asphyxiation (fig. 5).

It has perhaps been the tendency in the past for practitioners and coroners to assume that sudden death in an infant is likely to be due to unnatural causes, notably suffocation, sometimes with the result that investigations have not included autopsy. From the present study, the author is in complete agreement with Davidson [1] that such examination is an indispensable routine; moreover it should include histological studies, for especially in infancy, organs which appear normal to the naked eye not infrequently show a well-defined lesion microscopically.

¹An unsuspected duodenal ulcer found in one case of bronchopneumonia was exhibited at the meeting.

Sudden Death in Infancy (A Preliminary Communication)

By LESLIE L. R. WHITE, M.B., B.Ch.,¹D.C.H.

Department of Pathology and Bacteriology, Welsh National School of Medicine, Cardiff

SUDDEN death in infancy presents a problem of considerable importance to the coroner and medico-legal pathologist. It also merits the interest of those concerned with child health, at least in so far as certain of the deaths are ascribable to accidental and presumably avoidable causes.

Source of material.—The term "sudden death" may be used with varying implications. For the purpose of the present study the criterion adopted was that death occurred unexpectedly, an antecedent state of illness being admissible, but only when there was no suspicion of impending decease. The cases studied were all subjected to post-mortem examinations at the Pathology Department of the Welsh National School of Medicine, during the period January 1941 to May 1948.

The yearly incidence of the autopsies performed during the period selected shows a steady and significant increase (Table I).

TABLE I

Year	1941-2	1942-3	1943-4	1944-5	1945-6	1946-7	1947-8	1948 Jan.-May
No. of cases	1	5	7	12	12	14	19	11

It would seem probable that this increase is to a large extent the result of greater cautiousness on the part of the practitioner and coroner, with more frequent appeal to autopsy in verifying the cause of death.

Post-mortem examinations were conducted on 81 cases of unexpected death occurring during infancy. The age distribution (fig. 1) reveals that nearly one-third of these took place

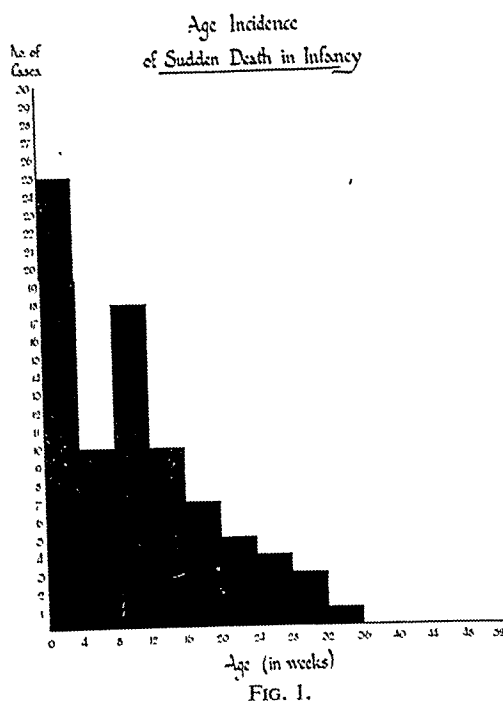


FIG. 1.

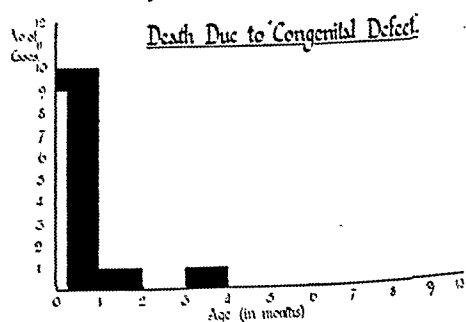


FIG. 2.

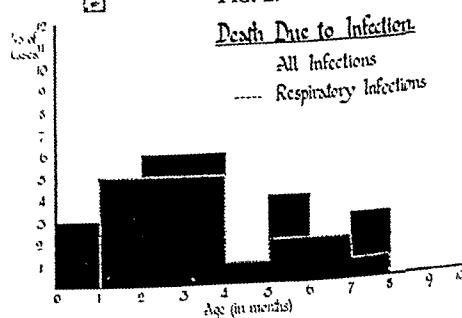


FIG. 3.

in the neonatal period and that thereafter there was a fairly uniform decrease in the incidence with increasing age.

A preliminary case analysis was made into four main divisions (Table II).

TABLE II

Cause of death	No. of cases	Cause of death	No. of cases
Infectious process	30	Mechanical suffocation	16
Aspiration of regurgitated food	23	"Congenital defect"	12

Section of the History of Medicine

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[December 3, 1947]

Charles Creighton, M.A., M.D. (1847-1927): Scholar, Historian and Epidemiologist

By E. ASHWORTH UNDERWOOD, M.A., B.Sc., M.D., D.P.H.

TWENTY years ago, on July 18, 1927, there died in a little cottage in the village of Upper Boddington near Rugby a man who had for eight years been regarded by the villagers with respect and affection. He never spoke of his life before he had come at the age of 70 to reside amongst them. Few—perhaps only one—of his former friends ever visited him. The man was Charles Creighton—described as the greatest medical scholar this country produced during the nineteenth century. Yet for nearly forty years he had been ostracized by the medical profession, not because of any crime or misdemeanour, but because he had dared to hold heterodox opinions on a procedure which in England is peculiarly liable to set the doctor and his patients off on different paths. When he died few voices were raised to pay him homage. *The Times* was discreetly silent. Professor William Bulloch, his oldest and most intimate friend, contributed sympathetic obituaries to the *Lancet* [1] and the *Aberdeen University Review* [2] and in the *British Medical Journal* Professor Greenwood [3] summed up in richly suggestive phrases the manner of Creighton's greatness. Eight months later Fielding Garrison in America contributed a more extensive review of Creighton's epidemiology [4]. He called his article "A Neglected Medical Scholar".



CHARLES CREIGHTON

That was twenty years ago. The object of this paper is not to review the work of Creighton in the detailed and critical manner which it undoubtedly merits. Its sole object is to point out that Creighton—to whom many have paid service from the lip and from the heart—is *still* neglected. Apart from the other writings of Professor Greenwood I have been unable to trace a single communication dealing with Creighton since Garrison's article in 1928. From one aspect that does not matter, since his best work has a lasting quality which defies time. But the man is part of his work, and the circle, never large, of those who knew Creighton in his lifetime shrinks at a dangerous rate as the years pass. It seems a safe bet that the man who wrote the book which Garrison refers to as the most considerable work in medical history which has yet come out of Great Britain will receive more than passing attention from the historian of the future. He will be interested in the *man*, as well as in the *History of Epidemics*. Except to a few the man is to-day a mere shadow. *Now* seems to be the time for those few to commit their recollections to print. The centenary of Creighton's birth is a fitting occasion to

make this appeal, and these remarks on his life and work are intended merely to drive this point home.

CREIGHTON'S EARLY LIFE

Charles Creighton, according to Bulloch, was the son of Alexander Creighton, a saw-miller and timber merchant of Peterhead. There Creighton was born on November 21, 1847. From the local school he went to the Gymnasium in Old Aberdeen. He gained ninth place in the bursary competition, and from King's College he graduated in Arts in 1867. His medical course was begun at Marischal College, but he seems to have finished

In occasional instances, however, autopsy results may lead to a mistaken presumption of mechanical suffocation, e.g. where an unobserved convulsion has occurred. In one instance a 2-day old baby was found at post-mortem to have visceral manifestations of asphyxia, with signs of facial pressure and anterior lividity. Death had actually taken place during a convulsion, and the signs suggesting suffocation from facial pressure were the result of subsequent deposition of the body in a package face-downwards. Had the convulsion not been noted death might have been attributed to mechanical asphyxia.

(4) *Death due to aspiration of regurgitated food*.—Twenty-three infants were considered to have died from asphyxia due to aspiration of regurgitated food (fig. 6).

Most pathologists would accept the finding of regurgitated material distributed throughout the lower airway as a sufficient explanation for asphyxial death. Simpson [2] has recently asserted that this is, in fact, a reversal of cause and effect, in that a state of asphyxiation induces vomiting, and subsequently inhalation of the vomitus may occur. He offers this theory without accompanying evidence.

It was noted in 10 cases, or nearly half of those with aspiration, that an underlying lesion was present which might reasonably be expected to produce vomiting rather than asphyxiation, viz. gastro-enteritis, otitis media, upper respiratory infection, &c. Further, though the series is admittedly a small one, the cases of undoubted mechanical suffocation (fig. 5) and those of aspiration of vomit show no correlation in age-incidence. Certainly many instances of asphyxia were unaccompanied by vomiting. Thus the evidence does not support Simpson's contention.

Another study of aspiration of vomit by Gardner [3] suggests that it is almost exclusively limited to artificially fed babies. He observes the small compact nature of the stomach of breast-fed infants at post-mortem and the liability to gross gastric distension in bottle-fed babies, presumably due [*sic*] to incidental aerophagy. Hence he deduces that an endeavour to regurgitate the gastric air-cap in the latter group leads to a possibility of inhalation of vomitus. In the present series, the mode of feeding was ascertainable in 12 out of the 23 cases showing aspiration and of these 4 were breast fed. Further, in those cases in which no underlying lesion was established (fig. 7) and where dietetic causes might possibly be of greater significance, 3 out of 7 cases were breast fed. Aspiration of stomach contents in breast-fed babies does not therefore seem to be a rare occurrence as Gardner has asserted. The apparently increasing incidence of aspiration of regurgitated food was the subject of a recent annotation in the *Lancet* [4] and subsequent correspondence [5, 6, 7] and certainly merits close attention, especially in view of the possibilities of preventing such a catastrophe. Regurgitation of food is prevalent in infants, but the factors leading to inhalation of the vomitus are as yet ill-defined.

Conclusion.—There appear to have been few extensive studies of sudden death in infancy, a problem which is of peculiar importance in relation to the present attempts to achieve further reduction in infant mortality. Detailed investigation and correlation of the social and pathological aspects are required, and for the latter it is essential to have the service of pathologists who are experienced in this branch of medico-legal work.

Summary.—(1) A preliminary study of the autopsy findings in 81 cases of sudden death in infancy is presented. (2) Of 30 deaths suspected from circumstantial evidence as due to overlaying, 9 were the result of mechanical suffocation; the remaining 21 were ascribable to other causes. (3) Asphyxia due to aspiration of regurgitated food as a cause of death is discussed.

The author is grateful to Professor Jethro Gough for his interest and helpful criticism, and for permission to make use of the autopsy records of the Welsh National School of Medicine, Pathology Department; also to Dr. A. G. Watkins, Pædiatrician to the Cardiff Royal Infirmary, for his encouragement.

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his training in Edinburgh. Having graduated M.B. at Aberdeen in 1871, he set out for the Continent, where he spent most of his time with Virchow in Berlin, and with Rokitsky and Skoda in Vienna. Virchow, at that time 50 years of age, was at the height of his powers as a pathologist and was active in the political field. Rokitsky was within four years of his retirement, and his dyscrasia theory was widely accepted. It is small wonder that, with the recollection of two such teachers in his mind, Creighton early decided to be a pathologist. Rokitsky indeed implanted his views so firmly in Creighton that they stuck with him during the remainder of his life. Creighton must have spent about a year abroad, and on his return he was successively medical registrar at Charing Cross Hospital, and surgical registrar at St. Thomas's Hospital. In 1873 he began work on cancer research under Burdon-Sanderson at the Brown Institution. I have been in touch with Professor Twort, who has very kindly gone through the annual reports and the correspondence of the Brown Institution from its foundation in 1871 to his appointment in 1909. No record of Creighton's name appears anywhere, and Professor Twort does not remember Creighton having visited the Institution after 1909 [5]. There is, however, some evidence [6] that he was really engaged by the Medical Department of the Local Government Board, to which John Simon was the medical officer. In 1874 there appeared in a volume of special reports of that department a communication of eighteen pages by Creighton [7]. It is entitled *Anatomical Research towards the Aetiology of Cancer*, and it deals with the earlier signs of cancerous invasion in the ultimate anatomical elements of the secondarily affected organs. The investigation involved a study of secondary tumours in the liver. In his preface to the collected reports Simon refers to this paper as "a contribution of much interest". This is the earliest paper by Creighton which I have been able to find. The *Index Medicus* was not started until five years later; there may be earlier papers, but I do not think there can be many. This paper seems to me to be a competent bit of work, bearing some traces of Virchow's influence. During the next two years Creighton had several other papers on physiological and pathological processes in the breast published in the Privy Council Reports, and these and certain other papers were collected to form his first book—*Contributions to the Physiology and Pathology of the Breast and its Lymphatic Glands*—which was published in 1878. He was then 31 years of age, and a brilliant and successful career was apparently just round the corner.

Meanwhile, in 1877, Creighton had been appointed Demonstrator of Anatomy at Cambridge under Sir George Murray Humphry. He was attached to King's College, of which Humphry later became a Professorial Fellow. The next few years in Creighton's life form an interesting exercise in speculation. In 1877, the year in which he went to Cambridge, he had an article "On the Development of the Mamma" in the *Journal of Anatomy and Physiology*. This was volume XI. Between then and the publication of volume XV for 1880-81 Creighton had ten more articles—a very respectable output. On the title page of volume XI for 1877 the editors are given as Humphry, Professor of Anatomy at Cambridge; William Turner, Professor of Anatomy at Edinburgh; Michael Foster, Professor of Physiology at Trinity College, Cambridge; and William Rutherford, Professor of the Institutes of Medicine at Edinburgh. For volume XII the editors were Humphry, Turner, and J. G. M'Kendrick, Professor of the Institutes of Medicine at Glasgow. For volume XIII (1879) the editors were Humphry, Turner and M'Kendrick; but a fourth editor was again added. This was Charles Creighton. Thus, at the age of 32, he had become a joint editor of a leading scientific journal, in very exalted company. For the next two years he remained a joint editor, and Cambridge University had meanwhile (1880) conferred the degree of M.A. *propter merita* upon him. He had certainly "arrived". Then, in 1881, he left Cambridge and came to London. No further papers ever appeared from his pen in the *Journal* after volume XV, and in volume XVI his name was dropped from the list of editors. A crisis had evidently occurred. Bulloch covers it with the phrase "He left Cambridge with some sort of a grievance and came to London". The crisis must have been great to warrant Creighton sacrificing such a brilliant future, and to encourage the editors to drop such an outstanding and enthusiastic colleague.

Creighton now came to London, and the Metropolis seems to have swallowed him up. He lived in it for thirty-seven years, and as the years went by he became more and more a shadowy figure, until many acquaintances had forgotten him completely. At first he tried general practice in Savile Row, and later in New Cavendish Street, but his attempt was unsuccessful. Bulloch, who knew him well for twenty years, said that "he was by nature totally unfitted for this branch of medical activity". During the greater part of his time in London—he left it in 1917—Creighton lived in chambers in Great Ormond Street. After his failure in practice he seems to have decided, possibly without reluctance, to devote himself to a life of literature and scholarship, and his time during this long period was divided between the British Museum, or some other great library, and his home. It was then that his great work was done. His last medical work during this period appeared in

1908—a book entitled *Contributions to the Physiological Theory of Tuberculosis*. During the next twelve years there was silence until, at the age of 73, he emerged from obscurity once again with *Some Conclusions on Cancer*—his last work.

SUMMARY OF CREIGHTON'S LABORATORY AND LITERARY WORK IN THE MEDICAL FIELD

In the following table I have grouped his writings to show the development of his thought and interests.

(a) Early pathological work ..	<ul style="list-style-type: none"> (i) Early papers: Privy Council, &c. (ii) <i>Contributions to the Physiology and Pathology of the Breast</i>, 1878. (iii) Other writings on the breast, cancer and bovine tuberculosis.
(b) Infectious disease and historical epidemiology.	<ul style="list-style-type: none"> (i) <i>On the Autonomous Life of the Specific Infections</i>, 1883. (ii) Translation of Hirsch's <i>Handbuch der historisch-geographischen Pathologie</i>, 3 vols., 1883–86.
(c) <i>Unconscious Memory in Disease</i> , 1886.	
(d) The vaccination question ..	<ul style="list-style-type: none"> (i) <i>Cow-pox and Vaccinal Syphilis</i>, 1887. (ii) <i>Encyclopædia Britannica</i>. Article on Vaccination, 1888. (iii) <i>Jenner and Vaccination</i>, 1889.
(e) The <i>Encyclopædia Britannica</i> (Ninth edition).	<ul style="list-style-type: none"> Articles on Malaria, Medicine, Morgagni, Pathology, Pellagra (Vaccination, see (d)).
(f) Historical epidemiology ..	<i>History of Epidemics</i> , 1891–4.
(g) History of public health ..	In Traill's <i>Social England</i> , 1894.
(h) Late pathological work ..	<ul style="list-style-type: none"> (i) <i>Formative Property of Glycogen</i>, 1896–9. (ii) <i>Cancer and Other Tumours of the Breast</i>, 1902.
(i) Plague	<i>Plague in India</i> , 1906.
(j) Tuberculosis	<i>Contributions to the Physiological Theory of Tuberculosis</i> , 1908.
(k) Cancer	<i>Some Conclusions on Cancer</i> , 1920.

I now propose to group these writings and to deal with some of them very briefly under a few headings.

(a) *Pathological writings*.—His earliest paper (1874) was concerned, as has been stated, with secondary growths in the liver. He reached a hypothesis that the secretory function of mucous membranes is performed by means of a process in the epithelial cells identical with the process known as endogenous cell-formation, and he thought this theory was of significance as regards the malignant tumours of epithelial parts. He took the mammary gland as an illustration of his theory, and his next papers were devoted to that gland. He first tackled the normal processes of development of the mammary function, involution and evolution, and then applied his results to what he called "the grand disease of the breast"—the tumour disease. He concluded that centres of different types of cancer cells may each infect with its own type of structure different glands in the same pocket. He admitted that this research had not taken him very far.

It would be fruitless to follow these researches further. Creighton always considered himself as a pathologist, and rated his pathological work higher than the historical researches which have made his name.

In the library of the Royal Society of Medicine there is a bound volume of reprints on pathological subjects by Creighton. A carefully written list of contents at the beginning of the volume is subscribed "C.C. June 1884" (see next page). This makes it fairly certain that the book belonged to him. So far this is one of the very few specimens of his handwriting which I have discovered.

To this group belongs the article on "Pathology" which Creighton contributed to the ninth edition of the *Encyclopædia Britannica*. This volume appeared in 1885. The article consists of 46 pages, and appears to be a competent piece of work. The preponderance of references to German pathologists, especially to Virchow, Cohnheim and their schools, is noteworthy.

The *Microscopic Researches on the Formative Property of Glycogen*, which he published in 1896, are of interest as illustrating one side of his character. From the preface he had obviously been refused a publication grant from some scientific body. He then turned to the Leigh Browne Endowment. This trust was founded "for the promotion of original research in the biological sciences without any recourse to experiments upon living animals"

Creighton's work was microscopic and did not involve animal experiments. Hence he had no hesitation in accepting the assistance offered.

(b) *Writings on tuberculosis*.—Creighton's early writings had dealt to a considerable extent with the pathology of bovine tuberculosis. In the tuberculosis field he was a heretic, out and out. His theories are now as dead as the dodo, but in any study of Creighton the man they are significant. Perhaps the best short statement of his early views is found in the *Encyclopædia Britannica* article on pathology. In referring to experiments to produce tuberculosis by inoculating or feeding tuberculous matter, he says that a suggestive proportion of all such experiments have succeeded. Then he goes on: "It has been boldly alleged by Koch that the active agent in the inoculative production of tubercle is not the tuberculous matter from a previous case, but a minute rod-like living parasite belonging to the order of schizomycetes. According to this view tubercle is from first to last an affair of a parasite". He then says that the weak point is that one cannot be assured that the inoculated parasites have been completely freed from the original tuberculous matter! This is a very good rock for a heretic to take his stand on.

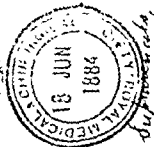
This article was published in 1885, and twenty-three years later Creighton was still fighting a magnificent rearguard action—though he would not have admitted, or even realized, that it was a rearguard action. It was a case of everyone else being out of step but himself. In 1908 he published his *Contributions to the Physiological Theory of Tuberculosis*. In this work he acknowledged the assistance of William Bulloch in obtaining for him inoculation material and the brains of patients who had died from tuberculous meningitis. He carried out a series of injections of tubercle bacilli into rabbits, and from the histological features he concluded that the resulting neoplasm was formed to get rid of the waste of disintegrated old blood corpuscles. He thought that bovine tuberculosis was a chronic disorder of nutrition, to which breeding might predispose in a very high degree. The same applied to a large part of human tuberculosis. As a cause of the tuberculosis of infants he suggested the absorption of milk from anæmic cows, which produced a state of the blood favouring the formation of minute multiple thrombi in the meningeal arterioles. There was nothing specifically infective common to human and bovine tuberculosis. He denied that tuberculosis was of the nature of a specific fever. Though cases of acute miliary tuberculosis often ran the course of a specific fever, it differed from other forms of tuberculosis only "in the insidiousness of the prodromata (in a scrofulous constitution) and the suddenness with which the actual crisis arises".

A man who could assert such views on experimental evidence in 1908, and have them published by a reputable publisher, must have been a very extraordinary character indeed.

(c) *Cow-pox and smallpox*.—Creighton's first work on this subject, *The Natural History of Cow-pox and Vaccinal Syphilis*, was published in 1887. There is no preface, and it is not clear when or for what reason he first embarked on the Jennerian question. In this work Creighton discusses the origin of vaccine lymph from the first stocks. He implied that Jenner had no justification for calling cow-pox "smallpox of the cow", and asserted that cow-pox had stronger relations with "the great pox" (syphilis) than it had with smallpox. He differentiated what he called "vaccinal syphilis" from "venereal syphilis" in the infant. In the following year Creighton's article on "Vaccination" appeared in the ninth edition of the *Encyclopædia Britannica*. Creighton re-emphasized his views on the identity of "vaccinal syphilis" with vaccinia of a severe type, and he regarded various sequelæ of vaccination—such as erysipelas, jaundice, skin eruptions, ulcers, and "vaccinal syphilis"—not as evidence of secondary infection, but as a reversion to type of certain manifestations produced by primary inoculation from the cow. Holding as he did such views regarding the nature of vaccinia and of vaccine matter, it was inevitable that Creighton should have cast doubt upon the practice of vaccination. This article, appearing in an authoritative publication which should, as a reviewer pointed out, have stood for a generation, raised much adverse comment in the medical press, and one reviewer stigmatized Creighton's views on the pathogenesis of cow-pox and of smallpox as "pathological transcendentalism". In the following year (1889) Creighton returned to the attack with his book on *Jenner and Vaccination: a Strange Chapter of Medical History*. Creighton was a tactician of a high order, and at the start of the book he proceeded to discredit Jenner's observational acumen. He suggested that Jenner's observation of the young cuckoo ejecting its foster brothers from the nest is a "tissue of inconsistencies and absurdities". Creighton then discussed the history of the whole question of vaccination in this country and in Germany, France and Italy. His concluding chapter summed up his views and gave more fuel to those who had called him an anti-vaccinationist. Greenwood [8] has reviewed the position from the modern aspect, and has shown that in respect of both the cuckoo and the fact that cow-pox is smallpox of the cow, Jenner was right and Creighton was wrong. A film has been taken of the cuckoo carrying out the ejection; and the work of Monckton Copeman and of Mervyn Gordon proved the analogy of smallpox and cow-pox.

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IX The Anatomical Basis of the Specific Infections of the Skin in the Dog, showing the Connection between Disorders of the Glandular Structures and Infection and Cancerous Degeneration of the Connective Tissues
Journal of Anat. & Physiol., Dec. 1879

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(d) *Historical epidemiology: Hirsch*.—The *Handbuch der historisch-geographischen Pathologie* was planned by August Hirsch about 1856, and the first edition appeared five years later. Though it was a monumental work a great mass of material was published in the following twenty years so that the second edition was a very large book. The first volume appeared in 1881, and Creighton was asked to undertake the translation of the whole three volumes for the New Sydenham Society. It was a Herculean task. The first volume of the translation appeared in 1883, and the second and third volumes in 1885 and 1886 respectively. Apart from indices the whole work in translation takes up over 2,100 closely printed pages. The volumes are heavily documented. Creighton must have learned a great deal in making this translation—but at a cost! He once told Bulloch that it occupied him for twelve hours a day for three years. If Creighton had done nothing else but this translation, he would still have placed the world of scholarship in his debt.

(e) *The History of Epidemics in Britain*.—The first volume of this great work appeared in 1891, and the second volume three years later. The whole work consists of over 1,500 pages; but even this number gives only a partial idea of the depth of its contents, and of the knowledge and labour which were essential for its compilation. Bulloch said that Creighton read and spoke every European language, alive or dead, and here we see the fruits of his remarkable ability.

The first volume covers the period from 664 to 1666, and deals with the following subjects in this order: Pestilences Previous to the Black Death; Leprosy in Mediæval Britain; The Black Death, 1348–49; Epidemics 1349–1485; The Sweating Sickness, 1485–1551; Plague in the Tudor Period; Gout Fevers and Influenzas in the Tudor Period; The French Pox; Smallpox and Measles; Plague and Fevers from James I to the Restoration; Sickness of Early Voyages and Colonies; The Great Plague of London.

The second volume covers the period 1666–1893, and has the following contents: Typhus and Other Continued Fevers; Fever and Dysentery in Ireland; Influenzas and Epidemic Agues; Smallpox; Measles; Whooping Cough; Scarletina and Diphtheria; Infantile Diarrhoea, Cholera Nostras and Dysentery; and lastly Asiatic Cholera.

It should be said that Creighton's peculiar views on the ætiology of infective diseases in no way impair the value of the work as a discussion of history. We meet these views very early in the book. On page 7 of the first volume he says that the nature of the plagues of 664 can only be guessed. "They have the look of having been due to some poison in the soil, running hither and thither, as the Black Death did seven centuries after". Somewhat further on he wonders whether the so-called psychopathies of the mediæval and more recent periods "may not have had a beginning, at least, in some toxic property of the staple food". These two factors keep recurring throughout the work, right up to the last outbreak of cholera. The stand which he takes sometimes leads him into a rather curious situation. For example, in discussing the plague-spots of the world, he gives six long quotations, dating between 1851–1882, from writers who had been to these places. In four out of the six there is *specific* mention of the mortality among rats, and even the results of post-mortems on rats. Two pages later he notes—correctly of course—that observations of rats leaving their holes during an outbreak are found in the plague books of London and Edinburgh during the Tudor period. He then says that this is only one of many proofs that the virus of plague has its habitat in the soils, although it may be carried long distances clinging to other things.

But such matters are extraneous. Among the great things in Creighton's work are his descriptions of the Black Assizes, his notable account of the history of variolation, his brilliant description of the results of the Black Death, and his numerous etymological references which indicate the true scholar. Among the latter is an interesting note on the derivation of the term "measles".

Of the two volumes of the work the first volume deals with a field which was practically untilled when Creighton entered it. His opening chapter is a most learned account of the famine fevers which were rampant in mediæval England, and in this chapter he embodied a mass of learning much of which had previously been available only in the original sources. There has been little research on this material since Creighton's day. His remarks on ergotism are especially interesting. The same may be said of his chapter on leprosy, in which he exposed a number of the misleading opinions of the day. The chapter on sweating sickness is of great importance. It was—and still is—the only comprehensive discussion of this strange malady. Creighton was able to discover a new document which fixed the date of first onset of this disease and which consequently had an important bearing on our knowledge of the sources of the disease.

Although the second volume, treating of the history of fevers since 1666, dealt with material which had already been written up in various forms, there is a mastery about Creighton's handling of the data which has so far discouraged all serious competition. There is too much important material in this volume to warrant selection for a short paper, but his

accounts of typhus fever and of influenza and epidemic agues are packed with information which is of practical interest to the modern epidemiologist.

The reviews of these volumes were uniformly good, but nearly all reviewers pointed out that, while Creighton's scholarship was almost beyond criticism, his views on the ætiology of infectious diseases must be disregarded. The *Lancet* said that it was a work which would without doubt "take the first rank, not only in medical, but in general literature". The reviewer concluded that "it is a great work—great in conception, in learning, in industry, in philosophic insight". To-day—more than fifty years after these words were written—modern scholarship can do nothing but endorse this view.

LATER LIFE AND INTERESTS

The controversy over cow-pox and vaccination was the great tragedy of Creighton's life. Although he must have been deeply hurt by the manner in which his professional colleagues received his views, he apparently did not show it. The years immediately following the start of the ostracism were of course full years: the great mass of historical material which he had accumulated during his years of reading in the British Museum was being arranged and the book written. He must at this time have been engaged also in writing the brilliant chapters on the history of Public Health which appeared in the volumes of Traill's *Social England*. These chapters still merit careful study. After the second volume of the *History* appeared in 1894 he wrote practically nothing in the medical field until 1896, when the first volume of his glycogen studies came out. The second volume appeared three years later. It would seem therefore that Creighton devoted five good years of his life to the prosecution of rather futile studies—handicapped as he was by the impracticability of carrying out experimental work on animals. I do not know where he had his laboratory, or where his microscopic work was carried out. Bulloch says that Creighton knew all about the latest methods of section-cutting and staining, and yet himself preferred sections cut with a razor from tissue embedded in a "penny dip", and stained with ink.

It was during these years in London that he made a habit, from about 1905 onwards, of looking in at the Bacteriology Department of the London Hospital about once every two months. Bulloch was of course the attraction. Professor Greenwood [9] tells me that Creighton was asked to give a series of lectures on the History of Medicine, and these were a great success. I have made enquiries at the London Hospital, and no record of this series is now in existence. Sir Paul Fildes [10] also knew him at the London Hospital at this period. He tells me that, though Creighton was a man who did not suffer fools gladly, he was in no way cantankerous. A brilliant conversationalist, he gave his juniors the impression that he was a friendly and unassuming man. Creighton must have been very lonely during these years, and he probably came to the London Hospital partly for that reason. His conversation during these visits would range over a variety of topics, but he was easily drawn on the subject of spontaneous generation, or on the tubercle bacillus. He professed great satisfaction in the fact that infectious disease was due to a miasma, and he was quite satisfied in his own mind that the tubercle bacillus, though present, was not the cause of tuberculosis. Professor Turnbull also knew him at this period, and he tells me that "however fantastic Creighton's views on some subject might appear to be at first, only a fool would not treat them with the greatest consideration. When they were carefully considered, it required very strong evidence to enable one to satisfy oneself that they were impossible" [11].

Creighton had a tall, commanding presence, and he was always meticulously dressed, with a turned-down Eton collar and a black satin tie passed through a ring.

SHAKESPEAREAN STUDIES AND OTHER LITERARY WORK

Creighton had been a student of literature all his life, and his immense learning and wonderful memory enabled him to range profitably over a wide field. He was deeply read in the Bible and in Shakespeare, and it was in this period—1904 to 1913—that his three books of Shakespearean criticism were published. *Shakespeare's Story of his Life* was published in 1904; *An allegory of Othello* in 1912; and *An allegory of King Lear* in 1913. In order to show the width of Creighton's learning and interests I propose to say a few words about the first of these books.

In 1900 Samuel Butler gave Creighton a copy of his book on Shakespeare's Sonnets, and Creighton soon disagreed—as he would do!—with Butler's identification of a key character in the sonnets. From the line in Sonnet 20 "a man in hew, all Hews in his controlling" Creighton identified Lord Herbert, and professed to confirm from other sources. He then said that the Sonnet series on the Rival Poet was occasioned by the death of Spenser, the Poet Laureate. The Rival Poet had been identified by Boaden as Samuel Daniel. Creighton agreed, and showed that though Daniel himself believed that he was the new Poet Laureate, he never got the patent for the office. The whole point is that Shakespeare, the greatest poet of his age, had been passed over, and the reasons are obscure. An answer is presumably

given in the next series of sonnets beginning "Farewell, thou art too dear for my possessing". Thomas Tyler had guessed that the lady addressed was Mary Fitton, a favourite maid-of-honour to the Queen, and Creighton proved this from other sources.

Creighton then found that from Sonnet 100 onwards there is an attempt to persuade Lord Pembroke to father an impending infant which is not his. Shakespeare was apparently impeached of the paternity—falsely as he alleged. Creighton followed this impeachment in various plays, and he devotes a special study to *The Tempest*, which is the story of Prospero's life. Creighton alleged that Lord Southampton had a hand in the early plays, and that Southampton was by way of being a poet. The plays had at first been anonymous, but while Southampton was abroad Shakespeare had begun to put his own name on the title pages. When Southampton returned he thought that he had been treated ill. Meanwhile Spenser died, and in Sonnet 94 Shakespeare discovers who had been plotting against him with reference to the succession.

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Section of Otology

President—DONALD WATSON, F.R.C.S.

[March 5, 1948]

The Evolution of the Auditory Conducting Apparatus

A New Synthesis Based on Functional Considerations

By A. TUMARKIN, F.R.C.S.Ed.

DEFINITION

THE auditory conducting apparatus comprises all those structures that enable an animal to pick up acoustic energy from its environment and to apply that energy to the auditory neuro-epithelium of the inner ear. It follows from the definition that any theory of the evolution of this apparatus must account not only for the auditory mechanism of the mammals, but also for the cruder structures found in lower animals to-day.

Mechanically, the conducting mechanism of the middle ear may be subdivided into:

(a) The collecting component (in mammals this comprises pinna, external auditory canal and tympanic membrane).

(b) The transmitting component (in mammals this comprises malleus, incus and stapes).

(c) The terminal component (the oval window and perilymphatic duct and fluid). Component (c) is dealt with elsewhere (Tumarkin [6]).

This paper deals with the evolution of components (a) and (b) and is based on an analysis of the conditions found in animals to-day.

Six main types may be distinguished:

(1) *V.Sq.*—*Vestibulo-Squamosal* (fig. 1A).—This is found in urodeles (i.e. the tailed Amphibia, e.g. newts, salamanders, &c.). The columella stretches from oval window to the squamosal. It is a bone-conducting mechanism. The animal picks up vibrations by direct contact between the skull and the substrate (i.e. ground or other vibrating material). There is no tympanic membrane and no middle-ear cavity.

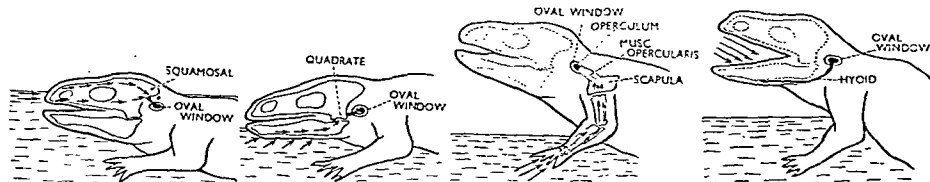


FIG. 1A.

FIG. 1B.

FIG. 1C.

FIG. 1D.

1A.—V.Sq. A primitive bone-conducting mechanism.

1B.—V.Q. A primitive bone-conducting mechanism.

1C.—V.S. An intermediate bone-cond. mechanism.

1D.—V.H. A primitive air-conducting mechanism.

(2) *V.Q.*—*Vestibulo-Quadrate* (fig. 1B).—Found in snakes—some lizards and many extinct reptiles. This resembles V.Sq. but the columella is attached externally to the quadrate. Vibrations are transmitted via the lower jaw and articulo-quadrate joint.

(3) *V.S.*—*Vestibulo-Scapular* (fig. 1C).—This remarkable mechanism is only found in urodeles and Anura (i.e. the jumping Amphibia, e.g. frogs and toads). It consists of an operculum, i.e. a plaque of cartilage lying in the oval window posterior to the true stapes. The musculus opercularis runs from the operculum to the scapula. Vibrations in the substrate pass via the fore-paw to the scapula and thence via the opercular structures to the vestibule. This is also a B.C. mechanism.

(4) *V.H.*—*Vestibulo-Hyoid* (fig. 1D), i.e. hearing via the buccal cavity and the hyoid bone. In amphisbaenids the stapes is continuous with the hyoid bone. These animals listen by opening the mouth. This is a crude form of air-conducted hearing. The floor of the mouth acts as a tympanic membrane and the hyoid acts as an intermediate ossicle comparable with the incus and malleus of the mammal.

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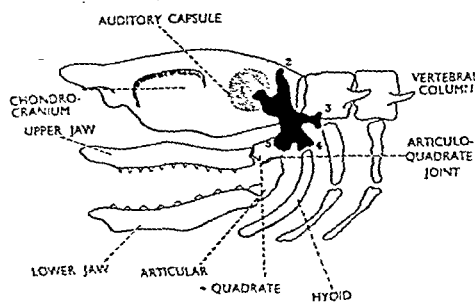


FIG. 3.—Cartilaginous fish skull showing five processes of hyomandibular. 1. Ventral process. 2. Dorsal process. 3. Opercular process. 4. Hyoid process. 5. Quadrate process.

the auditory capsule thinned out to form an oval window and the perilymphatic duct was laid down. The history of the auditory conducting mechanism really starts with the appearance of these two structures.

In addition to a ventral process the hyomandibular possessed:

A dorsal process extending up to the dermal skull bone (especially the squamosal).

A quadrate process extending to the quadrate.

A hyoid process extending to the hyoid.

The opercular process extending to the operculum. [This operculum is a scale-like bone overlying the gill-slits of the fish. It has no relation at all to the cartilaginous operculum of the amphibian oval window.]

It follows that vibrations would reach the auditory capsule along the following routes:

(a) Via the dermal skull bones and the dorsal process as the animal thrust its head in the mud.

(b) Via the lower jaw and articulo-quadrate joint and the quadrate process when the jaw was resting on the ground.

(c) Via the opened mouth and the hyoid and the hyoid process.

(d) Furthermore these animals were not *completely* deaf to sound waves impinging directly on the body surface. A small fraction of the sound striking the gill area would enter and pass via the opercular process to the ventral process.

(e) Lastly vibrations passing from the substrate into the manus and pectoral girdle would proceed via the crano-scapular muscles to the auditory capsule without the intermediation of the hyomandibular. Thus the primitive Amphibia received faint auditory sensations via five distinct routes, of which the first three were the most efficient.

Then followed a process of specialization in which one or other route was perfected at the expense of the others. Route (a) gave rise to the V.Sq. mechanism of modern urodeles. This is obviously an unambitious mechanism only suited to completely prostrate animals. Even the lowly urodeles have found it inadequate for the obvious reason that it ceases to function as soon as the head is lifted off the ground. They have therefore developed the next available route for detecting substrate vibrations, i.e. via the fore-paw. It appears therefore that the V.S. mechanism developed phylogenetically after the V.Sq. mechanism in response to the functional demands of a more erect posture. Generally speaking modern urodeles possess both V.Sq. and V.S. but the relative importance of the two mechanisms varies greatly. In the completely prostrate types V.Sq. predominates and V.S. may not be present at all. On the other hand in the more erect types V.S. predominates and V.Sq. tends to disappear entirely.

The primitive Amphibia flourished throughout the Devonian and Carboniferous but in the Permian they were being thrust into the background by the newly evolved reptiles.

For our present purpose it will suffice to describe the main stem reptiles (the cotylosaurs) branching off into the archosaurs the pro-squamata and the premammalians (see fig. 15).

The archosaurs gave rise to the mighty dinosaurs who dominated the earth all through the Mesozoic era. They became extinct in the Cretaceous but early offshoots are represented

(5) *V.T.*—*Vestibulo-Tympanic*, i.e. hearing via a perfected drum and a single ossicle. In the highest Amphibia, i.e. frogs and in most reptiles, e.g. crocodiles, turtles, and many lizards, the stapes (usually called the columella) is a delicate spicule of bone lying freely mobile in a middle-ear cavity. Its inner extremity fits into the oval window—its outer extremity is continuous with a cartilaginous extra columella, which is inserted into a perfected trilaminar drumskin.

(6) *V.O.*—*Vestibulo-Ossicular*.—This is the mammalian triple ossicle system.¹

In addition to these clear-cut mechanisms, certain transitional types must be included. *Sphenodon*—a primitive New Zealand lizard shows the transition from *V.H.* to *V.T.* The stapes in this animal is still continuous with the hyoid—but in addition it sends a process to a plaque of fibrous tissue which lies subjacent to the pharyngeal mucosa. This plaque is largely overlain by the *musculus depressor mandibulae*, so that it can hardly pick up external sounds, nevertheless we shall see that certain primitive animals, starting with *V.H.* evolved *V.T.* and in the process passed through a stage similar to *Sphenodon* (see fig. 5).

It appears that other lizards have evolved from *V.Q.* to *V.T.* and so it is still possible to find amongst the various agamid and iguanid lizards all stages in this transition. In some the stapes is firmly attached to the quadrate. In others a rudimentary drum has formed but it is still overlain by muscles. In others the muscles have receded but the drum is still overlain by scales. *Pari passu* with this evolution of the drum goes the development of the middle-ear cavity. The stapes itself becomes thinner, and instead of being enveloped by muscles and connective tissue, it gradually becomes airborne being merely suspended by a thin mesentery of mucous membrane (fig. 6).

THE SYNTHESIS

It remains to correlate these data with each other and with the known facts of paleo-biology.

We start therefore at the Devonian era with the evolution of the amphibia. At that time the climate was torrid. The earth was covered with steamy lagoons which were liable to dry up periodically. Under those circumstances, the fish in them died. Gradually in response to such periodic disasters the stegocephalian Amphibia emerged, able to breathe air when necessary and provided with four limbs which enabled them to crawl off in search of water.

The very earliest Amphibia such as *Eogyrinus* (fig. 2) closely resembled the fishes except

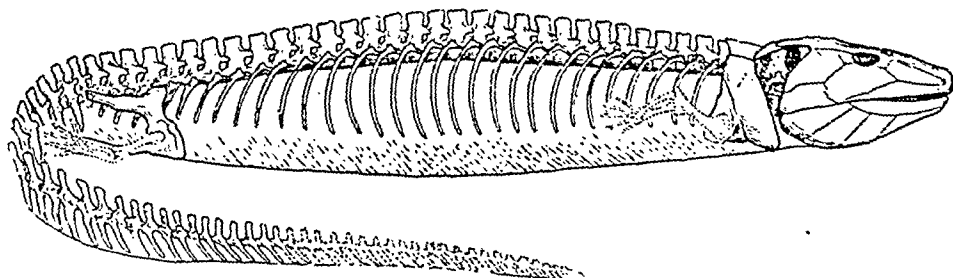


FIG. 2.—*Eogyrinus*, a Carboniferous embolomere amphibian; estimated length about 15 ft. (After Gregory, modified from Watson.) (Reproduced by permission.)

that they had four flabby little paws in place of fins. They lived mostly in water, only venturing on to land when the shallow lagoons dried up. In water the animal was enveloped by an environment of almost identical characteristics. A sound wave traversing the water easily entered the skull. On land, however, it was surrounded by air. But sound waves in a gaseous medium like air when they encounter a dense medium like a fish are almost completely reflected. Therefore the amphibian was very deaf to airborne sounds. There was, however, another avenue for sound transmission, the ground. These primitive Amphibia were prostrate and sound waves in the ground easily entered their bodies. At that time there was no specialized acoustic receptor. The utricle and saccule were purely organs of static equilibrium. It is clear however that these structures—primarily acting as gravity receptors—would also respond to the periodic vibrations of a sound wave. It was this biological accident which evolved an acoustic receptor out of the primitive gravity receptor.

¹In (1) (2) (4) (5) and (6) the nomenclature is based on the attachments of the stapes. The internal attachment in each case is to the vestibule (i.e. the oval window). The external attachment completes the titles. *V.O.* for instance indicates that externally the stapes articulates with an ossicle, i.e. the incus. In (3) the operculum determines the nomenclature.

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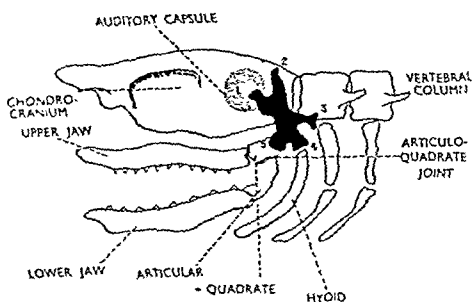


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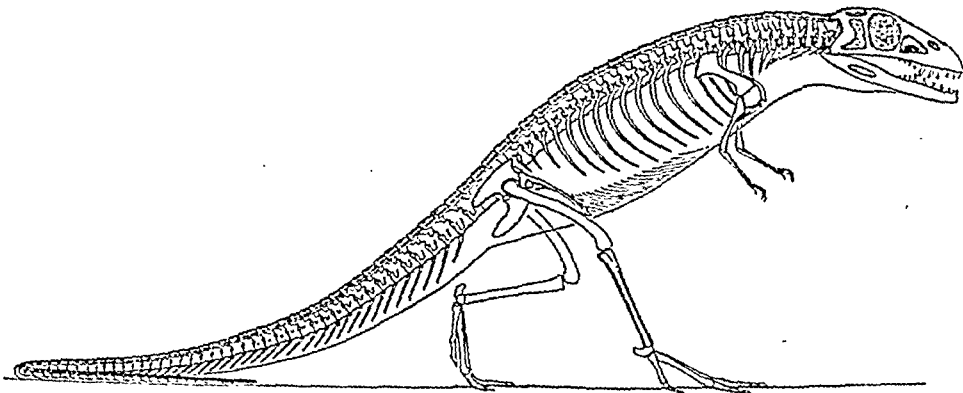
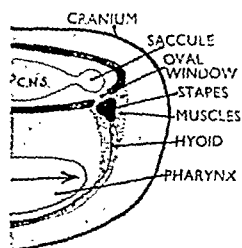


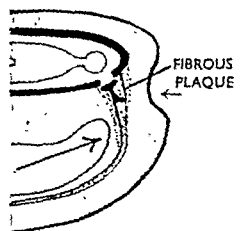
FIG. 4.—*Saltoposuchus*, a lightly built Triassic thecodont, about 3½ ft. in length. (From von Huene.) This animal obviously rarely had its skull or fore-paw on the ground. Therefore it had no use for V.Sq., V.Q. or V.S. hearing. It almost certainly had airborne hearing comparable to that of *Sphenodon*—or it may even have achieved perfect V.T. hearing. (Reproduced by permission.)

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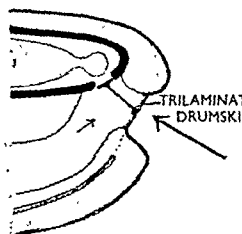
The pro-squamata apparently started off with route (b) (i.e. V.Q.) and in fact snakes still use that route. Most lizards have evolved V.T. out of V.Q. as shown in fig. 6 but certain species have not advanced as far as others. It is in fact possible to demonstrate in modern lizards all stages of evolution from the primitive V.Q. to the perfected V.T.



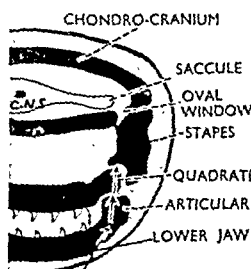
Stage I.—V.H. as found in amphibienids. The stapes is a solid conical mass overlain by muscles and articulating with the hyoid. Arrows indicate path of sound conduction (a).



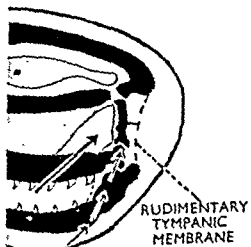
Stage II.—V.H. + rudimentary V.T. Present in *Sphenodon*. The stapes has become smaller. It is still connected with the hyoid but it also sends a process to a plaque of fibrous tissue in the overlying muscles. The animal still mainly hears via the mouth but the plaque is faintly sensitive to external airborne sounds (b).



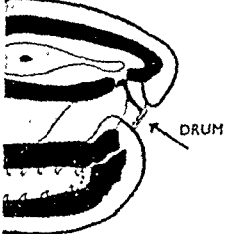
Stage III.—Perfected V.T. The stapes is extremely delicate and airborne. A true tympanic membrane is present. The middle ear opens widely on to the pharynx (c).



Vestibulo-quadrato.—Note massive stapes overlain by muscles and articulating firmly with quadrate. Arrows indicate path of sound conduction (a).



V.Q. + rudimentary V.T. as in *Lyriocephalus*. Note the rudimentary tympanic membrane in the masticatory muscles. The stapes is smaller. The epipharynx sends a pouch towards it (b).



Perfected vestibulo-tympanic. The muscles have receded. The drum has reached the surface. The stapes is delicate and airborne (c).

FIG. 5.—The transition from vestibulo-hyoid to vestibulo-tympanic hearing.

FIG. 6.—The transition from vestibulo-quadrato to vestibulo-tympanic hearing.

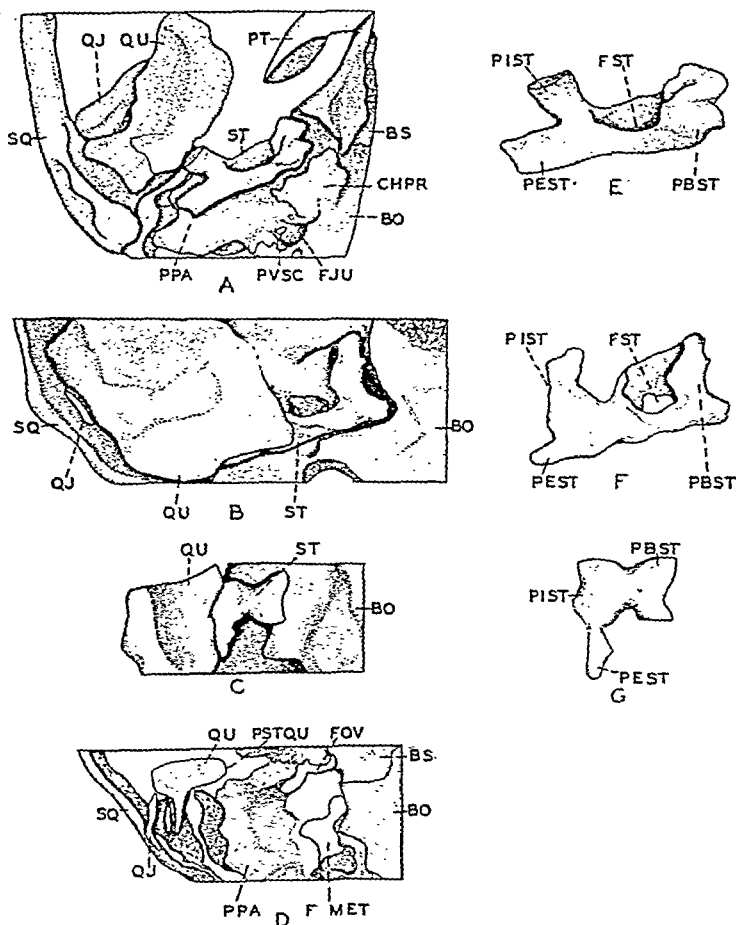


FIG. 7.—The therapsid stapes. Ventral views of right tympanic regions and stapes of selected therapsids. Reconstructed from wax models and from sections. A. Therocephalian B, *Tapinocephalus* zone. B. Gorgonopsian B, *Cistecephalus* zone. C. Anomodont E, *Endothiodon* zone. D. Cynodont B, horizon uncertain. Right stapes of three therapsids in ventral aspect. Drawn from wax models which were reconstructed from sections. E.—Therocephalian B. F.—Gorgonopsian B. G.—Anomodont E.

Note the relatively enormous size of the stapes. In each case the bone is so firmly locked to adjacent bones—especially the quadrate—that a tympanic membrane would have been entirely useless. (From *Spec. Papers Geol. Soc. Amer.*, 1944, No. 55, p. 40, by permission.)

The pre-mammalian reptiles utilized V.Q. also. Fig. 7 shows the skulls of some typical therapsids. The stapes is a massive structure firmly articulating with adjacent bones—in particular with the quadrate. It is obviously impossible for such a stapes to have been energized by the feeble flapping of a tympanic membrane and we must deduce that the pre-mammalian reptiles utilized V.Q. bone-conducted hearing, just as the pro-squamata did. Nevertheless they did not evolve in the same way, the fact being that the modern mammalian middle ear differs from the reptilian in possessing three ossicles in place of the single columella of the reptile.

The explanation of the mammalian triple ossicle system is to be found in the amazing metamorphosis of the jaw-joint. The mammalian lower jaw consists of a single bone—the dentary, which articulates with the squamosal. In all other terrestrial vertebrates the lower jaw consists of 6 or more elements—the dentary, splenial, angular, surangular, articular, &c. This complex bone articulates with the quadrate at the articular and we have to consider how the primitive articulo-quadrate joint became supplanted in the mammal by the squamoso-dental joint. The reasons why this change occurred are not clearly understood, but one

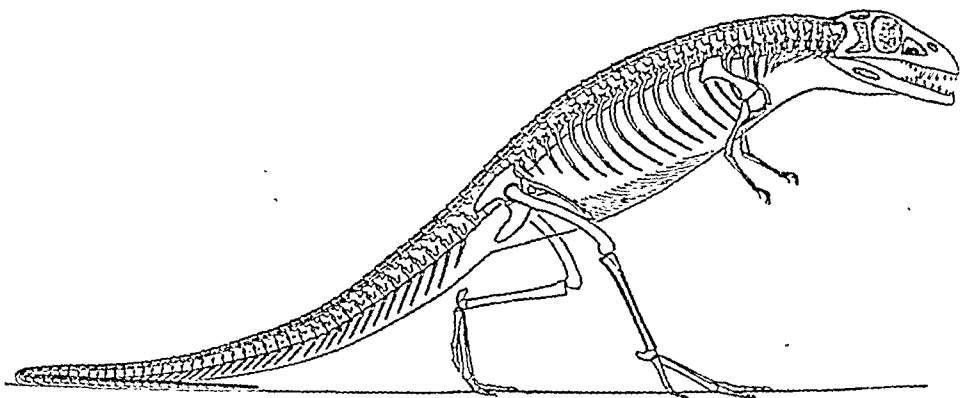
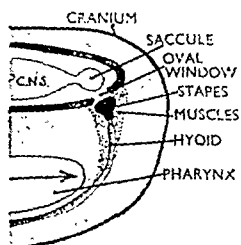


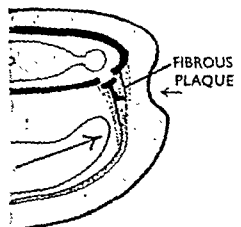
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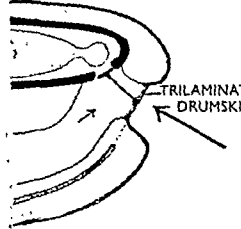
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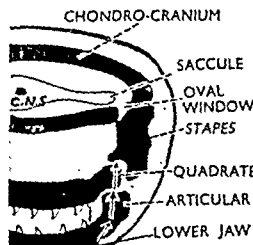


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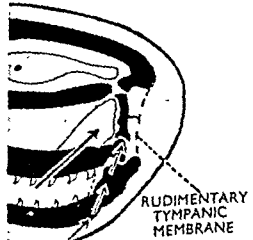


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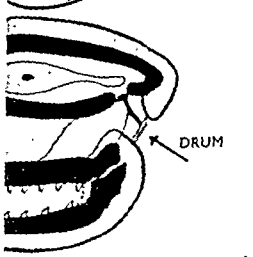
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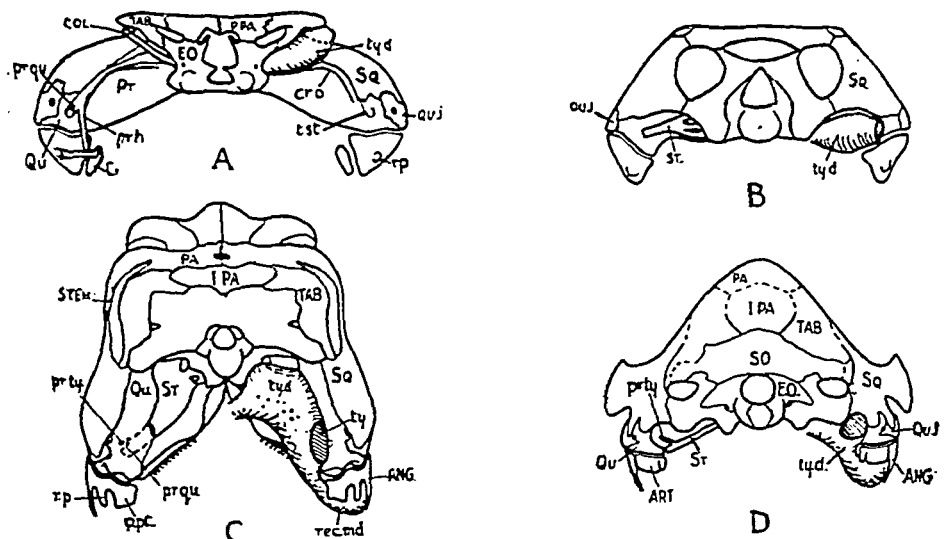


FIG. 10.—Attempted reconstructions (schematic) of tympanic diverticula in fossil tetrapods.

A, the stegocephalian *Benthosuchus*, adapted from Bystrow and Efremov. B, the cotylosaur *Dimetrodon*, adapted from Captorhinus, adapted from Sushkin, Price and others. C, the pelycosaur *Lycedops*, adapted from Romer and Price. D, the therapsalian *Lycedops*, adapted from Broom. In each figure the columella auris or stapes is shown on the left side, the tympanic diverticulum on the right. Col—St—Columella (or stapes). Ty.d.—Tympanic diverticulum. ty—Tympanic membrane. Qu—Quadrate. Sq—Squamosal. (From T. S. Westoll, *Proc. roy. Soc. B.*, 1943, 131, 393.)

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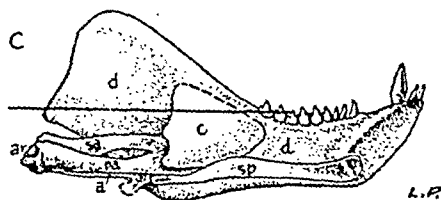


FIG. 8.—Lower jaw of *Cynognathus*—internal aspect. ar—articular. a—angular. d—dentary. sa—surangular. pa—pre-articular. (Reproduced by permission.)

Fig. 8.—shows the inside of the lower jaw of cynognathus. It still articulates at *ar*, the articulo-quadrate joint, but obviously the dentary is reaching upwards towards the base of the skull. It is easy to envisage a stage at which a squamosal-dentary bursa would develop externally to the primitive joint, the jaw, actually rocking on a double articulation. Subsequently the squamoso-dental-joint took over full function and the articulo-quadrate joint was completely superseded. The subsequent transition may be described in a few words (fig. 9). The ossicles became progressively lighter and at the same time the pharyngeal mucosa pushed outwards whilst the skin pushed inwards.¹ The two layers approximated to form the typical trilaminar drum. In the process the articular was trapped together with the adjacent fibrous tissue and that explains how the handle of the malleus (which is derived from the articular) persists in the substance of the tympanic membrane. Similarly, the tympanic annulus would develop out of the posterior jaw-bone element to which the fibrous tissue in question was attached, i.e. the angular. Thus the tympanic membrane of the mammal has developed along completely different lines from either that of the Squamata or of the archosaurs.

There is still another type of tympanic membrane to be discussed, that of the Anura. We left the urodeles at the stage of the V.S. mechanism having noted that in some types (e.g. Triton) the hyomandibular columella has completely disappeared, the animal depending solely on V.S. The Anura seem to have travelled functionally along a similar path to that of the Urodela.² Some toads, like Bombinator, only possess an opercular mechanism; like Triton, they have no columella whatsoever. We assume, therefore, that the Anura in general passed through a stage in which only V.S. was present, but the more progressive frogs went further and developed a V.T. mechanism as well. If, however, the hyomandibular columella had by that time completely disappeared it would not be available to produce the anuran columella. Therefore the latter must have developed out of some other structure. In other words it is not homologous with the hyomandibular-derived columella of the urodele. Evidence in support of this will be adduced later (see fig. 13).

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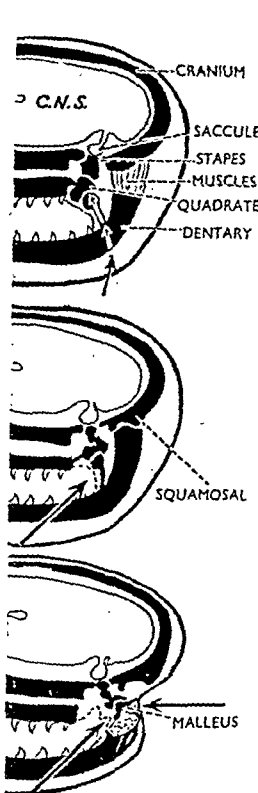


FIG. 9.—The development of the triple ossicle system.

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Vestibulo - quadrate hearing in *Cynognathus*.

The dentary has reached the squamosal to form the mammalian joint. The reptilian joint is superseded. The ossicles are shrinking in size. The animal opens its mouth to listen.

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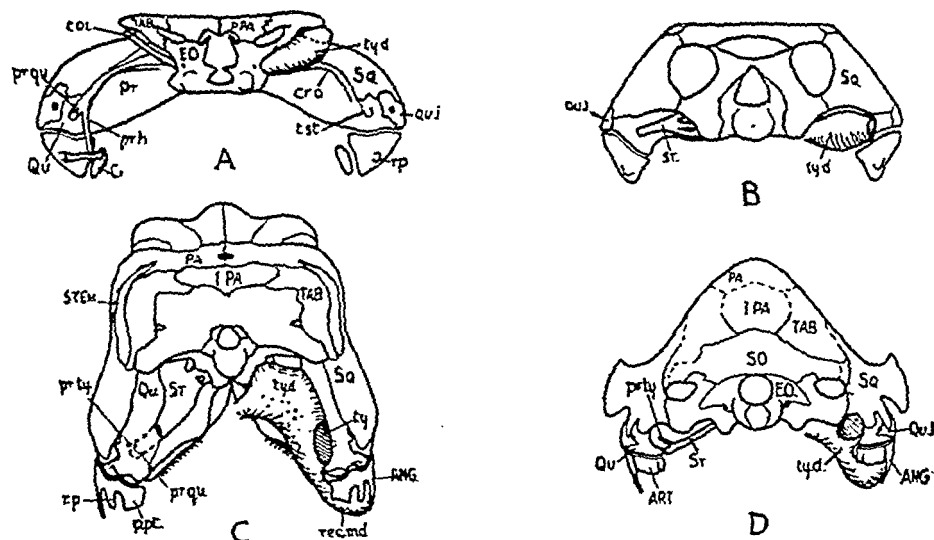


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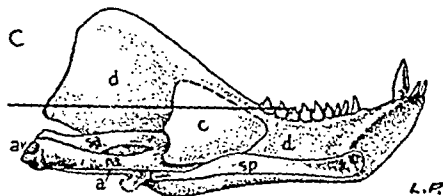


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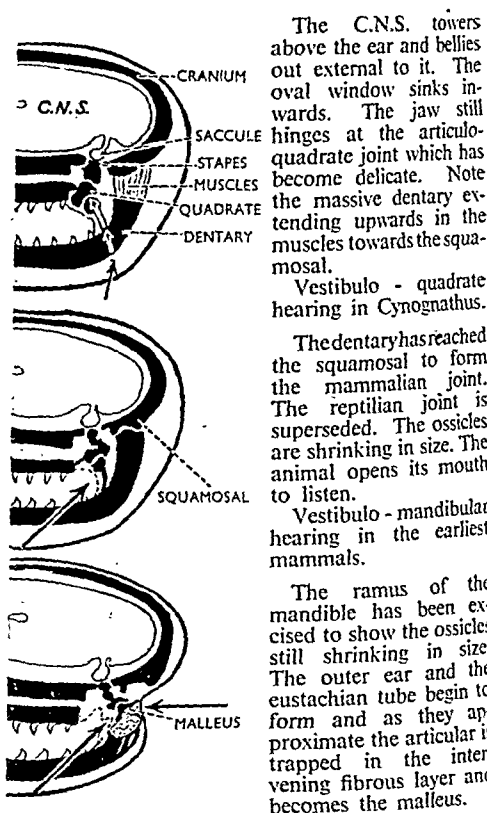


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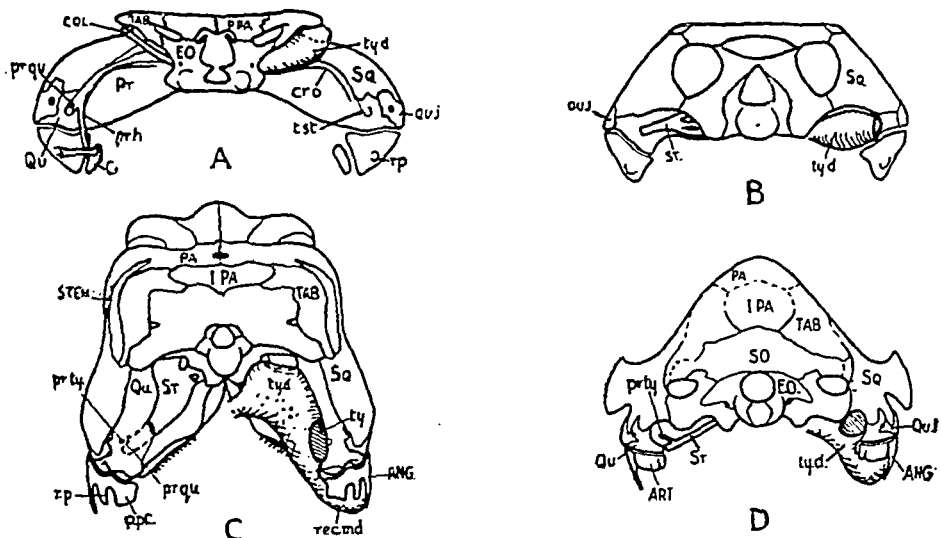


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points to the otic notch. It is difficult to avoid the conclusion that morphologists have merely assumed that a drum and tympanic cavity must have been present. Having located the stapes they quite uncritically postulate a middle-ear cavity and drum to go with it. The tabulosquamosal notch at first sight is a suitable situation for a drum but actually there is strong evidence that it did *not* house a tympanic membrane. This notch is quite prominent in very early Amphibia (e.g. *Ichthyostega*) in which the oval window had not yet evolved. The writer has shown [7] that in the absence of an oval window a tympanic membrane could have had no possible function. Thus on functional grounds it must be stated that the otic notch did not house a tympanic membrane. It has been argued that the slender nature of the stegocephalian columella is evidence that it was airborne. This is entirely fallacious. Fig. 12 shows the stapes of *Lyriocephalus*, a modern lizard. It is a long slender stylus (with a small cartilaginous extra columella) strongly reminiscent of the stegocephalian. *Lyriocephalus* possesses no true tympanic membrane or cavity and there is no reason to believe that the *Stegocephalia* did. Certainly the mere appearance of the bony structures does not justify the assumption.

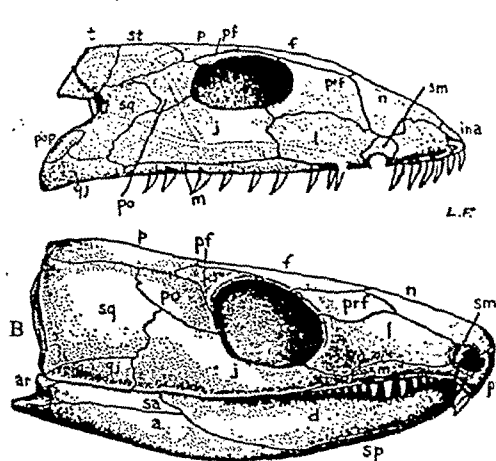


FIG. 11.—A: Lateral view of skull of *Ichthyostega* showing otic notch. B: Lateral view of skull of *Captorhinus* showing absence of otic notch.

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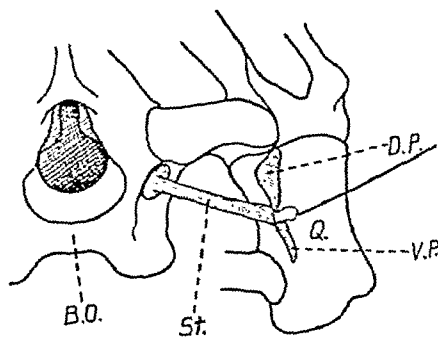


FIG. 12.—Hind view of skull of *Lyriocephalus scutatus*. This modern lizard has no drum or middle-ear cavity. The dorsal process (D.P.) and ventral process (V.P.) are attached to the quadrate. A small cartilaginous extra columella enters the superjacent muscles. The arrangement closely resembles fig. 10 and illustrates the fallacy of assuming the existence of a drum or middle-ear cavity solely from the appearance of the bony skeleton. (From *Evolutionary Changes in the Middle Ear of Certain Agamid and Iguanid Lizards*, by Malcolm A. Smith, *Proc. zool. Soc. Lond. Ser. B*, 1938, Part 3, 1938, by permission.)

Septicism as to the otic notch is, if anything, increased by a consideration of the cotylosaurs. These stem reptiles more or less supplanted the Amphibia and gave rise subsequently to the mighty radiation of the Mesozoic reptiles. One would expect them in general to have improved on the Amphibia, but actually the cotylosaurian stapes is a massive bone bound firmly to adjacent structures, in particular the quadrate. It seems unquestionable that the cotylosaurs heard by V.Q. Despite this, orthodox theory persists in ascribing to them a middle-ear cavity and a drum as in fig. 10b. The precise situation of the drum is unspecified. As shown in fig. 11b the otic notch has disappeared and it is apparently presumed that the cotylosaurian drum lay somewhere in the soft tissues near the jaw-joint. This is a remarkable transition. Mechanically speaking the otic notch would have been an excellent situation for a drum. If the *Stegocephalia* had really achieved such an excellent tympanic annulus it seems incredible that the cotylosaurs could have abandoned it. Yet this is implicit in the orthodox theory which states that the otic notch was obliterated by a downspreading of the adjacent bones—without considering the functional implications.

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In the writer's theory these difficulties and dilemmas do not arise. It is recognized that a tympanic membrane of sorts may have existed in close relation with the lower jaw of the therapsids—but it was not the delicate trilaminar drumskin of the orthodox theory. It was merely the fibrous tissues which enveloped the obsolescent articulo-quadrate joint. The later therapsids had vestibulo-mandibular hearing and not V.T. It is true that this "tympanic membrane" was at the mercy of the mandibular muscles just as is that of *Sphenodon* to-day. It was indeed a crude structure, nevertheless it was more efficient than the V.Q. mechanism of the pelycosaurs, cotylosaurs and Stegocephalia which preceded it. Thus, in the writer's theory, the transition from amphibian to reptile was accompanied by a process of improvement such as would be normally expected to occur and there was no disastrous migration from otic notch to lower jaw such as is implicit in the orthodox theory.

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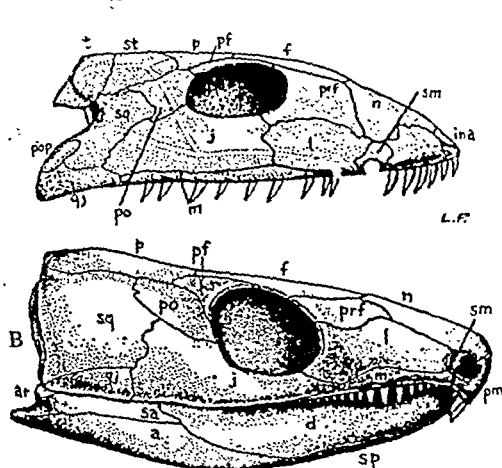


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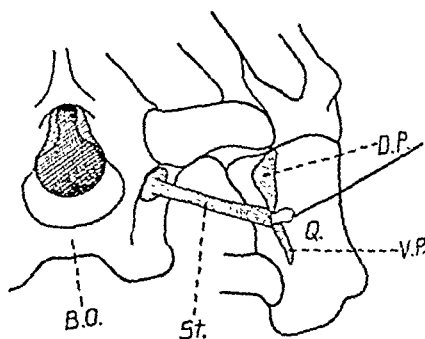


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The functional theory thus postulates a progressively improving mechanism—the transition being from V.Q. to V.M. and so to V.O. In this transition the obsolescent articulo-quadrate structures play a useful part and their incorporation in the mammalian ossicular chain follows logically. Orthodox theory on the contrary provides no explanation for the incorporation, and indeed the usual account involves a retrogression as disastrous as that of the stegocephalian-therapsid transition. We are asked to believe that the therapsids enjoyed adequate V.T. hearing which they had inherited from the cotylosaurs and that somehow the obsolescent articulo-quadrate structures forced themselves between the stapes and the tympanic membrane. This means that at some stage the stapes became dissociated from the tympanic membrane. No suggestion is made as to why this should have happened.¹ It seems to be a most unnatural conception involving grave loss of efficiency.

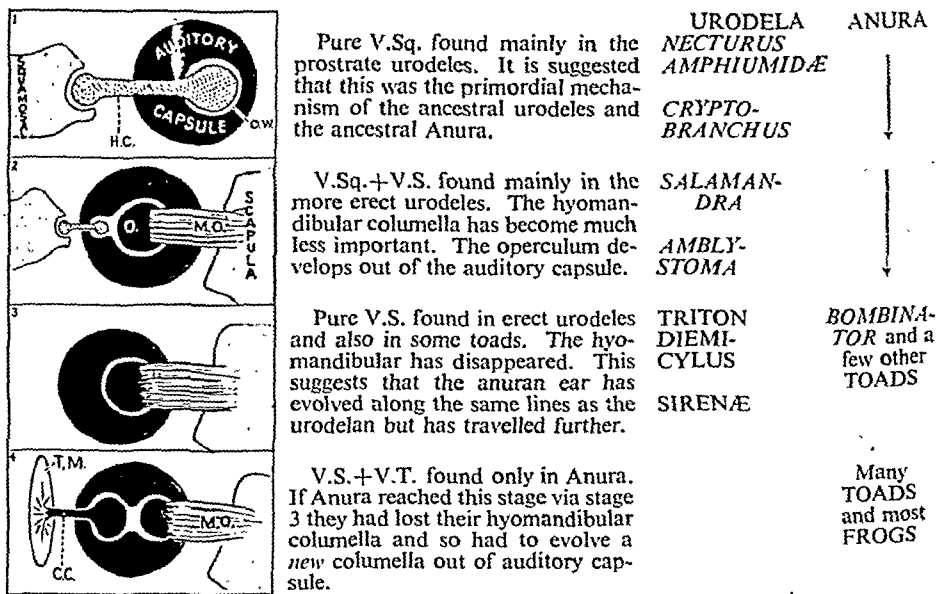


FIG. 13.—The auditory mechanism of modern amphibia.—V.Sq., V.S. and V.T. (Functional theory).

Functional theory suggests that modern Amphibia represent various stages in evolution. Orthodox theory declares that modern Amphibia represent various stages of degeneration.

H.C. Hyomandibular columella.

M.O. Musc. opercularis.

O.W. Oval window.

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The functional theory is further confirmed by the embryological order of appearance of these various structures. If it is correct to declare that the phylogenetic order was urodele columella first, then operculum, then anuran columella, we expect to find that order preserved in ontogeny. On the other hand orthodox theory, identifying the urodele columella with the anuran, requires them both to appear embryologically before the operculum. Kingsbury and Reed have shown quite definitely that the urodele columella precedes the operculum, whilst the anuran columella succeeds it.

The urodele columella is derived from the hyomandibular although even so it is not to be regarded as identical with the columella either of the Squamata or of the archosaurs.

¹It should be noted that physically speaking the triple ossicle mechanism is in no way superior to the monossicular system so that nothing was gained from the interpolation.

THE PHYLOGENY OF THE AUDITORY CONDUCTING MECHANISM (ORTHODOX THEORY)

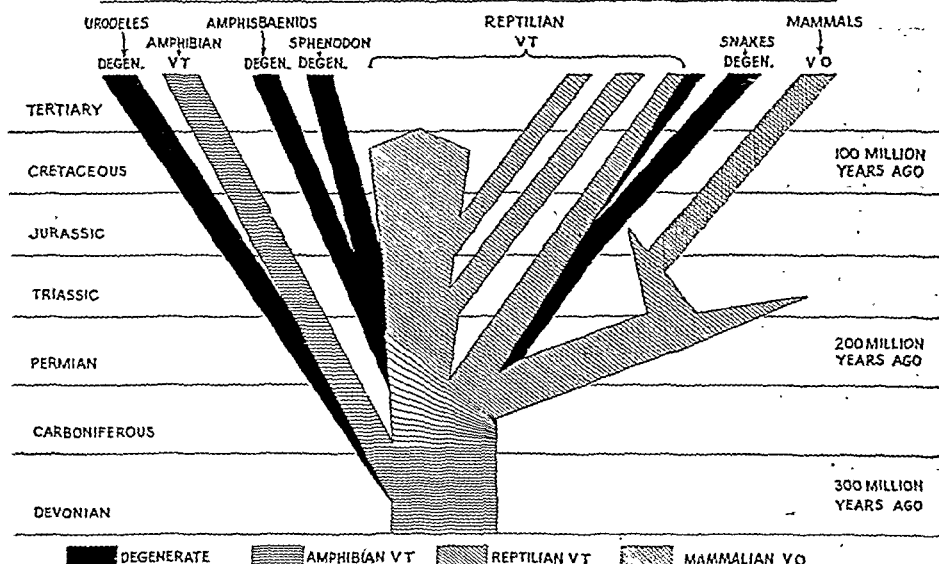


FIG. 14.—A tympanic membrane is postulated in the stegocephalian "otic notch". Modern frogs have inherited it. Urodeles, amphisbaenids, snakes, Sphenodont and many lizards are degenerate. The cotylosaurs modified the stegocephalian mechanism by transferring the drum from the otic notch to the articulo-quadrato region. Mammals separated the drum from the columella and thrust the articulo-quadrato complex into the gap. See fig. 15 for details of primitive reptilian groups.

THE PHYLOGENY OF THE AUDITORY CONDUCTING MECHANISM (FUNCTIONAL THEORY)

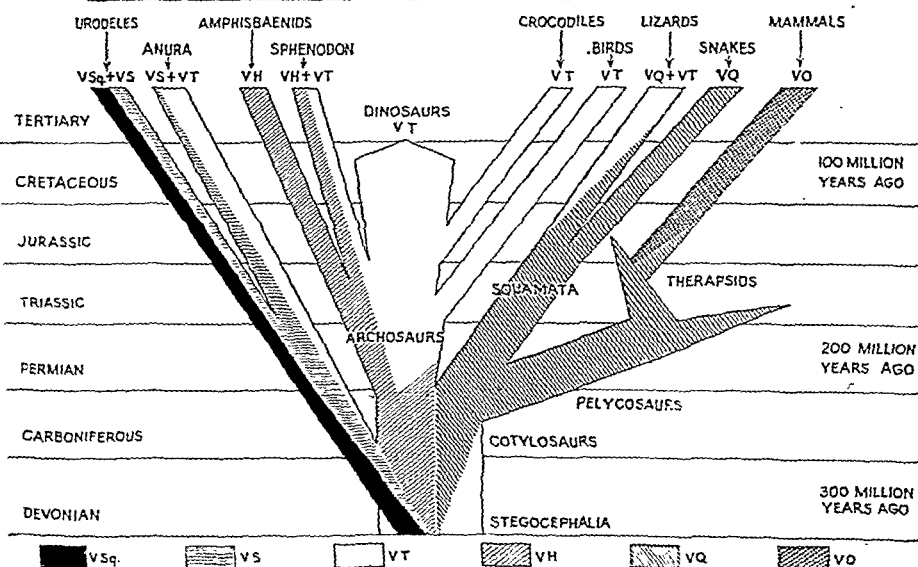


FIG. 15.—The Stegocephalia started with rudimentary V.Sq., V.Q. and V.H. V.S. was also "potentially" present. Urodeles specialized in V.Sq. and later added V.S. Anura went on to add their own special type of V.T.

Cotylosaurs had V.Q. + V.H.

Archosaurs show the transition V.H.→V.T.

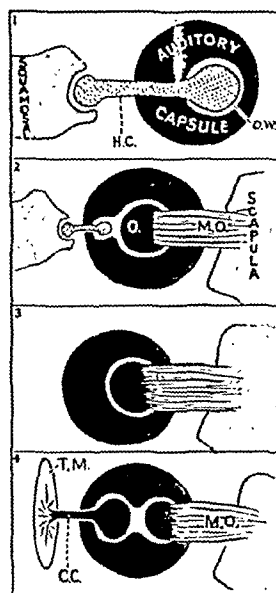
Squamata show the transition V.Q.→V.T.

Mammalia show the transition V.Q.→V.O.

Acknowledgments.—Figs. 2, 4 and 8 are reproduced by permission from "Vertebrate Paleontology" by A. S. Romer, 2nd ed., 1945, Chicago. Figs. 7, 10, 11 and 12 are reproduced from other sources, details of which will be found below the illustrations concerned.

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Pure V.Sq. found mainly in the prostrate urodeles. It is suggested that this was the primordial mechanism of the ancestral urodeles and the ancestral Anura.

V.Sq. + V.S. found mainly in the more erect urodeles. The hyomandibular columella has become much less important. The operculum develops out of the auditory capsule.

Pure V.S. found in erect urodeles and also in some toads. The hyomandibular has disappeared. This suggests that the anuran ear has evolved along the same lines as the urodele but has travelled further.

V.S. + V.T. found only in Anura. If Anura reached this stage via stage 3 they had lost their hyomandibular columella and so had to evolve a new columella out of auditory capsule.

URODELA ANURA

NECTURUS
AMPHIUMIDÆ
CRYPTO-
BRANCHUS

SALAMAN-
DRA
AMBLY-
STOMA

TRITON
DIEMI-
CYLUS
SIRENÆ

BOMBINA-
TOR and a
few other
TOADS

Many
TOADS
and most
FROGS

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The differences may be tabulated as follows:

Functional theory		Orthodox
Urodele columella	Ventral + dorsal processes of hyomandibular	} VENTRAL PLUS OPERCULAR PROCESS OF HYOMANDIBULAR
Archosaurs columella	Ventral + hyoid processes of hyomandibular	
Squamata columella	Ventral + quadrate processes of hyomandibular	
Anuran columella	Auditory capsule	

In seeking for further evidence to enable us to choose between the two theories we turn to the neural relations. The facial nerve is closely related to the primitive hyomandibular. It emerges from the auditory capsule between the ventral and dorsal processes. Orthodox morphologists regarding all columellæ as identical expect to find them preserving identical relations with the facial nerve. Unfortunately this is far from being the case. Whereas in urodeles the main trunk of the nerve is *below* the columella, in all other animals it is *above*. Textbooks offer no explanation of this paradox, but the functional theory explains it quite simply. It is exactly what we should expect when we observe that V.Sq. of urodeles utilizes the dorsal process of the hyomandibular, i.e. the only process which is dorsal to the nerve. All the other processes are below it.

Again the chorda tympani in the Anura is post-tympanic—in all other animals it is pre-tympanic. This paradox has never been satisfactorily explained by the orthodox theory. On the functional theory it simply does not arise. The anuran columella is a totally different structure from all other columellæ and there is no reason to expect it to maintain identical relations. Figs. 14 and 15 show the two theories diagrammatically.

SUMMARY

The orthodox theory of the evolution of the middle ear is criticized for the following reasons:

- (1) It is based too exclusively on palæontological and ontological evidence.
- (2) In virtually ignoring the functional implications it accepts hypotheses which are "unreasonable" on physical and physiological grounds.
- (3) It labels organs as homologous on inadequate evidence and in the face of much evidence to the contrary.

(4) It adheres to the outdated conception that homologous organs must of necessity be inherited from a common ancestor.

(5) It is exclusively preoccupied with the airborne type of middle ear. Much standard work is devoted to the problem of locating the site of the tympanic membrane. Such work is doomed to failure because the tympanic membrane in many cases did not exist as such. The drum is phylogenetically a comparatively late development and was preceded by at least 5 other auditory mechanisms.

(6) These other mechanisms (V.Q., V.Sq., V.S., V.H. and V.M.) are mechanically comparatively crude but biologically they must be placed on a par with the air-conducting mechanisms V.T. and V.O. They are alternative solutions to the problem of picking up acoustic vibrations which confronted the primitive amphibian when it first floundered on to land.

(7) Orthodox theory has no place for these alternative mechanisms and is reduced to dismissing them as "degenerate."

(8) An alternative theory is proposed in which due regard is paid to the functional implications. This leads to many deductions which are diametrically opposed to orthodox theory. It appears that this functional theory not only conforms satisfactorily to all the available ontogenetic and phylogenetic data but it also disposes quite easily of the various paradoxes which render the orthodox theory so unacceptable.

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